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THE EFFECTS OF BILATERAL STELLATE GANGLION BLOCK ON MENTAL DEPRESSION

Report of 3 Cases

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The idea of attempting to alter cerebral function by interruption of the sympathetic nerves to the cerebral blood vessels is not a new one. As early as 1899 Alexander[1] and in 1896 T. Jonnesco[2] performed cervical sympathectomy in the treatment of epilepsy.

More recently Mixter and White, as reported by White and Smithwick[3] in 1941, carried out bilateral cervicothoracic sympathectomy in a series of patients with severe epileptic seizures but found that the final outcome was disappointing.

Dandy[4] in 1931 reported his experience in the treatment of migraine by sympathectomy, as did Craig,[5] and Love and Adson.[6]

Royle[7] in 1932 described his experience in the treatment of a number of cerebral diseases by resection of the cervicothoracic sympathetic ganglia. However, Royle's previous writings on the relief of spasticity by sympathetic ramisection had been so thoroughly discredited that this contribution attracted little attention.

In 1943 and again in 1946 Risteen[8] and Volpitto[9] reported favorably on the use of stellate ganglion block in cases of cerebral vascular occlusion and other neurologic disorders.

During the past year our interest in attempts to influence cerebral physiology by interrupting the cervical sympathetic nerves has been aroused. In January, 1946, a woman, aged 38, was observed with complete left hemiplegia of five weeks' duration due to cerebral embolus. This patient had excruciating pain in the entire paralyzed side. There was such extreme dysesthesia of this side that the patient would scream when the skin was lightly touched. She presented a serious nursing problem because she would not tolerate any movement. Her discomfort was considered to be of thalamic origin. Since vascular occlusion in an extremity is usually associated with some degree of vascular spasm, it was considered possible that the thalamic pain in this case might be due to an associated cerebral vascular spasm. In an effort to relieve this

presumed cerebral vascular spasm it was decided to block the sympathetic nerve supply to the brain. Accordingly, on January 16, 1946, the right stellate ganglion was injected with novocaine. The patient exhibited a prompt physiologic response with a Horner's syndrome and increased temperature and dryness of the right side of the face and right upper extremity. There was no relief, however, from pain in the left side. In order to exclude a crossed sympathetic innervation to the thalamus, the left stellate ganglion was then similarly injected but again with little or no immediate relief. However, after the patient returned to her hospital room she developed very definite relief of her discomfort, and by the following day her thalamic pain had entirely disappeared and has not recurred.

Since the above experience, bilateral stellate block has been performed in a series of patients with cerebral vascular disease, brain atrophy, and parkinsonism.* In some instances where it was deemed indicated, the novocaine block was followed by surgical interruption of the sympathetic nerve supply to the brain. These patients were frequently enthusiastic about the improvement which these procedures afforded them. But when motion pictures were made of the patients before and after treatment it was found that the actual improvement in motor function was relatively slight. We finally realized that what was being accomplished in these patients was that we were producing an alteration in their mood.

Most prominent and most constant responses in patients subjected to interruption of the sympathetic outflow to the brain were subjective experiences expressed in terms of greater sense of animation, self-security, and a feeling of well-being which often approximated euphoria. In general this subjective improvement overshadowed objective benefits, and one gained the impression that the patients performed better in motor and mental capacities because they felt better. In reviewing the previous status of these patients it was noted that the greatest display of elevated mood was found in those whose cerebral lesion was associated with a definite pre-existing mental depression.

The elevation of mood in these organic states was sufficiently impressive to suggest to us the use of bilateral stellate procaine block in individuals suffering with involutional melancholia, depressive states, extreme anxiety neuroses, and schizophrenia.

* *In performing these injections the technic de Sousa Pereira has been found to be free of complications as well as being simpler and more certain than other methods. (de Sousa, Pereira A.: Blocking of middle cervical and stellate ganglions with descending infiltration anesthesia; technic, accidents and therapeutic indications. Arch. Surg.* **50**:152-165 (*Mar.*) *1945.*)

Three case histories are presented to emphasize the more concrete features of this reaction in depressed patients to temporary interruption of sympathetic impulses to the brain.

Case Reports

Case 1. A minister's wife, aged 44, was examined on March 7, 1947. She complained of episodes of fatigue and dejection which had appeared during the previous October. At the time she expressed the opinion that she was an evil woman who had "sinned against God". She talked in an apathetic manner, had a marked psychomotor retardation, and reiterated that she had committed many errors and was utterly useless as a wife to a devoted husband. She stated that she had failed signally in helping him in his church work and set a bad example to the members of his congregation.

She had had a depressed state in 1932, from which she completely recovered after a period of nine months in a psychiatric hospital. In 1946 she was operated upon for a herniated intervertebral disk, during which ordeal she manifested no evidence of mental depression.

Bilateral stellate block was performed on March 7, 1947. One-half hour later she proffered a spontaneous smile and announced that the weight of feeling that she was going to perdition for her sins had suddenly lifted. "I have no sense of sin, everything seems so different now. I now realize that it was my attitude that made me feel as I did and that it was not the neighbors' denunciation of me, nor was it my operation which caused me to feel so low." She recalled all her feelings of being sinful and frankly could not understand how she could have entertained such ideas less than an hour before.

In contrast to her previous state of apathy and retardation, she was sprightly in manner and wholly alert in her answers and recitals of her subjective improvement, which persisted for two days.

Case 2. A married man, aged 35, presented himself at Cleveland Clinic because of nervousness and depression on April 21, 1947. Two months before, he had become apathetic, exhausted, had lost interest in his work, and could not sleep. His appetite and sexual libido had suddenly waned. He became self-condemnatory in terms of sex inadequacy, schooling, and retro-rationalized his present condition by attributing it to auto-eroticism in his youth. He had frequent crying spells, entertained ideas of futility, and hinted at suicide.

In 1936 he had had a long episode of depression, from which he eventually recovered. During the war years he was in active military service and was discharged with an excellent conduct record.

Bilateral stellate block was carried out on April 23, 1947. Immediately after the physiologic effects were observed he openly grinned, something which his wife had not observed for several months. He asserted suddenly that he no longer felt like jumping out of the Clinic window, as he had contemplated doing an hour before. At the moment of complete sympathetic block, which was more pronounced on the left side, he had a sudden feeling "as if the world became lighter and brighter". "It seems as if I have a little more courage to do the things we had planned to do. I do not feel over-elated, but I just feel that now I have a chance. I hope this will never wear off." His wife, who is a nurse, pronounced the change as a "miracle" and happily exclaimed that "this is the man I really married".

The transformation persisted for two days. He whistled at home, on the first night he went to sleep spontaneously and awoke with high spirits. The feeling of well-being or normal cheerfulness (euthymia) persisted well over seventy-two hours.

Case 3. A man, aged 49, who led a busy life as a building contractor, was first examined on March 4, 1947. He stated that he had become progressively depressed for the past month and came to the conclusion that his brain was no longer functioning. His wife testified that he had frequent crying spells, was extremely unstable, very despondent, and was unable to concentrate on his work. He predicted dire disaster for himself and his business, felt that he was no longer useful to himself or to his community, and had definite surges of suicidal impulsion.

In the past history it was revealed that he had had a sharply delimited episode of depression, nervousness, and insomnia during 1942. He was given shock treatment for a period of seven weeks and completely recovered his normal joviality and animation.

We found him to be in an abject degree of depression and suggested shock treatment. He was in such agony of indecision that he refused to consider this therapeutic program and argued that it was useless to do anything for him because his case was utterly hopeless.

A bilateral stellate block was performed on March 5, 1947, with 10 cc. of 1 per cent novocaine injected into each side. He developed a bilateral ptosis of mild degree, an immediate contraction of both pupils, and increased warmth of both hands.

His first reaction was to announce that his memory was suddenly keener, and he was able to recall six numerals which had been presented to him one minute before. He announced that he was more objective about his depression. Most edifying was his feeling that he could make decisions with more promptness and security and that his concern about the future was not so great. His psychomotor tempo was decidedly increased. He ceased having crying episodes, which were well demonstrated an hour before the block, and expressed the feeling that he could now proceed with shock therapy without hesitation.

The euphoria persisted very definitely for three full days, after which time he was not so brisk and self-secure but still maintained that his mind was better, that he could think better, and "the extreme melancholy has been taken away from me".

The positive and favorable effects of bilateral stellate ganglion block in patients with true endogenous depression, such as involutional melancholia or the depressed phase of manic-depressive psychosis, develop with the appearance of the Horner syndrome and anhidrosis of the face. Some patients report a preliminary sense of flushing on the side of the head ipsolateral with the site of injection. After the procedure is completed on both sides the facial expression usually becomes animated by a spontaneous smile. The dejection, the sense of futility, the agony of indecision, the tendency to self-depreciation and self-denunciation so characteristic of the melancholic state give way to a general sense of well-being and to a normal self-estimation. Two patients after injection recollected with puzzlement and amazement the morbid content of their ideas and obsessions which were entertained but a few minutes before. The freedom from morose mood and its concomitant morbid ideation was a striking subjective experience acutely appreciated by several subjects and usually was announced without solicitation.

In general, physical animation accompanies the psychic acceleration. Normal sleep and appetite reappear in striking contrast to the long, pre-existing period of insomnia and anorexia.

Naturally all these benefits are short-lived. The duration of mood enhancement in these cases did not extend beyond seventy-two hours after procaine block.

In patients who proffered "depression" as one of many other symptoms and whose condition was patently psychoneurotic, the procedure of stellate block did not produce either a heightened affect or a relief from the subjective tensions. From this it would appear that blocking of the sympathetic nerve supply to the brain may offer a therapeutic test for differentiating the deep anxiety psychoneuroses from truly endogenous depressions, being similar in this respect to electric shock. To be most effective, both stellate ganglia should be blocked at the same sitting. It is our present opinion that the alteration in mood is due to some factor other than cerebral vasodilation.

Two schizophrenic patients, both in hebephrenic regression, were subjected to bilateral cerebral sympathectomy by resection of the superior cervical ganglia. Here again the results were practically barren of any modification or enhancement of affect, and the psychotic behavior was in no wise modified.

Summary

Temporary block of sympathetic impulses to the brain by procaine injection of both stellate ganglia in 3 patients suffering with endogenous mental depression induced a heightening of affect, a relative euphoria, and a transitory relief from morbid ideation and psychomotor retardation.

No such affective reaction was obtained by applying the same technic to psychoneurotic patients, to schizophrenic subjects, or to patients without cerebral or mental disease.

The effect of stellate block on depressed mood suggests that the sympathetic outflow to the brain plays a role in contributing to the cenesthetic or mood level of consciousness. Amplified studies are indicated in order to determine whether sympathetic interruption to the brain through surgery will permanently modify the cyclic behavior of the affective reaction psychoses and whether it can in some cases replace prefrontal lobotomy in the treatment of chronic depression which has proved refractory to shock therapy.

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PEPTIC ULCER IN MECKEL'S DIVERTICULUM

Report of a Case

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Intestinal hemorrhage constitutes the essential symptom of peptic ulcer in Meckel's diverticulum. The blood is usually passed as fresh blood or clots from the rectum, but at times the stools may be tarry. Hemorrhage may occur suddenly and be the only symptom, or it may be preceded or followed by abdominal pain. Pain is the only other symptom in this condition. However, unless the inflammatory changes about a chronic ulcer have reached the visceral peritoneum, there is no pain, rigidity, or tenderness, but there may be a colic-like distress variously described as vague, cramp-like, or gnawing. It usually bears no relation to meals but often may be referred to the umbilicus.

Nine cases of bleeding from the bowel proved at operation to be due to a Meckel's diverticulum have been seen at Cleveland Clinic in the past fifteen years (table). All but 1 patient had bleeding from the rectum. This was a 4½-month-old baby boy who had bloody fecal drainage from a fistula at the umbilicus. Four patients complained of pain, varying from mild abdominal distress in the region of the umbilicus to cramps in the lower part of the abdomen with nausea and vomiting. Seven patients were male. Six patients were under 25 years of age, the average in this series being 21.3 years. Although peptic ulcer of Meckel's diverticulum is said to be an affliction of childhood, no age group is immune.

The following is a detailed report of our most recent typical case.

Case Report

A boy, aged 4½ years, was admitted on April 1, 1947. He had been well until five days prior to admission, when at his normal habit time in the evening he had had a bowel movement which contained a considerable amount of bright red blood. On the following evening he had a large black tarry stool and two days later had several tarry stools. There had been no pain or other associated symptoms. The parents had noted his increasing pallor after the appearance of the tarry stools.

Physical examination revealed a well developed boy of 4½ years with pronounced pallor. The remainder of the physical examination was essentially normal. There were no petechial spots. Examination of the abdomen revealed no tenderness or rigidity, and digital rectal examination was negative. Special blood studies showed a decided secondary anemia with 1,990,000 red blood cells and 33 per cent hemoglobin. The white blood count was 9450, and the differential count was normal. The icteric index, platelet count, bleeding, and clotting times were normal. Proctoscopic examination for 12 cm. revealed normal findings. However, the stool coming from above was tarry black.

The patient was given six small whole-blood transfusions of 125 to 200 cc. each. On the fourth hospital day a laparotomy was performed, and a Meckel's diverticulum was found 3 feet above the ileocecal valve. The diverticulum measured 3 inches in length and contained a fresh globular blood clot about 1.5 cm. in diameter. On microscopic section gastric mucosa was noted in the tip, and a small ulcer was identified at the border of the gastric and intestinal mucosa. The patient was discharged on the seventh postoperative day.

TABLE

Case	Age	Sex	Symptoms	X-Ray	Surgery	Pathology
1	39 yrs.	M	Recurrent dark red blood from rectum—4 years	G.I. series neg.	Meckel's diverticulum 36″ above ileocecal valve	Ileal and gastric mucosa. *Ulcer identified*
2	4½ yrs.	M	Recurrent dark red and tarry stools—5 days	None	Meckel's diverticulum 36″ above ileocecal valve	Ileal and gastric mucosa. *Ulcer identified*
3	3½ yrs.	F	Recurrent umbilical cramp-like pain with nausea and vomiting. Recurrent bright blood in stools—2 years	G.I. series neg.	Meckel's diverticulum 8″ above ileocecal valve	Normal ileal mucosa. *Ulcer identified*
4	4½ mos.	M	Fistula at umbilicus with bloody fecal drainage since birth. Some nausea and vomiting	Fistula to small bowel	Patent duct leading to a Meckel's diverticulum	No report
5	3 yrs.	F	Recurrent abdominal pain, nausea and vomiting, bright blood in stools—2 years	None	Meckel's diverticulum 21″ above ileocecal valve	Ileal mucosa and gastric mucosa. Pancreatic tissue also
6	38 yrs.	M	Recurrent pain in left side—16 years. Recurrent blood in stools—5 months	G.I. series neg.	Meckel's diverticulum 36″ above ileocecal valve	Ileal and gastric mucosa
7	25 yrs.	M	Recurring hemorrhages of bright red and dark clotted blood from rectum—5 years	None	Meckel's diverticulum 30″ from ileocecal valve	Normal ileal mucosa

TABLE — Continued

Case	Age	Sex	Symptoms	X-Ray	Surgery	Pathology
8	17 yrs.	M	Recurring pain in lower abdomen with several silent rectal hemorrhages of bright red blood—5 years	G.I. series neg.	Meckel's diverticulum 18″ above ileocecal valve attached to umbilicus	Normal ileal mucosa with gastric and duodenal mucosa
9	60 yrs.	M	Recurrent dark red blood from rectum—2 weeks	G.I. series neg.	Meckel's diverticulum 18″ above ileocecal valve	No report

In those cases in which an ulcer crater was not found serial sections of the diverticulum were not made. None of the patients have had a recurrence of symptoms.

Meckel's diverticulum represents a remnant of the intestinal end of the omphalomesenteric duct. In the embryo, after differentiation of the primary alimentary canal from the yolk sac, the intestinal canal is blind at the cephalic and caudal ends, but the midgut portion is continuous with the yolk sac. The opening into the yolk sac gradually narrows as the anterior abdominal wall closes in, but the midgut retains a connection with the diminishing sac by a slender tube, the yolk stalk, also known as the vitellointestinal or omphalomesenteric duct. As the yolk sac degenerates, the stalk exerts traction on the midgut at the point of attachment, drawing a loop of bowel out of the body cavity into the umbilical cord. Normally the bowel returns to the abdomen by the tenth week of intra-uterine life, and the umbilicus is the last point in the abdominal wall to close. According to Meckel, an arrest in the development of the small intestine when it is still in connection with the umbilical vesicle may give rise to several grades of maldevelopment. In the most severe grade a fissure remains in the abdominal wall below the umbilicus, through which the ileum opens. The lower part of the bowel may be very narrow or closed, and feces may pass through the opening at the umbilicus. In the next grade the abdominal fissure persists, with the ileum in direct communication with the opening at the umbilicus by means of a patent ductus omphalomesentericus. However, the small intestine is well developed, and feces pass on into the colon (case 4). In the next grade the ventral fissure is closed, but a blind process of the

ileum is present, united to the umbilicus by the obliterated duct, which is represented as a solid fibrous cord (case 8). In the next grade the omphalomesenteric duct remains as a free diverticulum from the ileum.

Meckel's diverticula vary greatly in length and shape. A mesentery similar to that of the appendix is usually present. The diverticulum is ordinarily located in the ileum between 30 and 90 cm. from the ileocecal junction and usually projects from the free border of the ileum.

A Meckel's diverticulum occurs without complication in from 1.5 to 3 per cent of all persons. It occurs most often (75 per cent) in the male sex. Fortunately, symptoms are rarely caused by this vestigial remnant, but it may be associated with complications which may prove serious. A perforation may result from impaction of a foreign body within the pouch. The diverticulum may be the seat of volvulus and gangrene. The diverticulum may form a noose or knot or become adherent within a hernial sac. Tumors of various types have been reported in the diverticula. The diverticulum may invaginate and cause intussusception. Harkins believes that about 17 per cent of Meckel's diverticula causing symptoms do so by producing an intussusception.

One of the most interesting features of Meckel's diverticulum is the frequent presence of heterotopic tissue in the diverticulum. This occurs in about 25 per cent of all Meckel's diverticula. The heterotopic tissue usually is gastric mucosa histologically analogous to the mucosa of the fundus and may, in addition, contain duodenal mucosa and/or pancreatic tissue. These diverticula which contain heterotopic gastric mucosa possess the potentiality of ulceration.

Numerous theories have been proposed to explain the presence of such aberrant elements in the diverticulum. The earliest and most commonly accepted theory is that of Albrecht (cited by Matt and Timpone), who maintains that the entoderm lining the primitive intestinal tube possesses the potentiality of developing into any of the glandular components of the fully developed gastrointestinal tract.

That these dystopic portions of mucous membrane in Meckel's diverticula do not merely resemble the mucosa of the fundus morphologically but are also functionally active has been amply demonstrated by analyses of their secretions in cases of open umbilical fistula. Both pepsin and hydrochloric acid have been detected by various observers. Furthermore, this secretion clearly begins or increases synchronously with the activity of the stomach and occurs at a time during which the small bowel is empty and when there is no neutralization by food and intestinal juice. Such a condition is especially favorable for the generation of peptic lesions.

Ordinarily the ulcer is situated within the area of the intestinal mucosa and relatively close to the boundary of the heterotopic gastric mucosa. The macroscopic and microscopic appearance of the ulcer closely resembles that of the typical gastric and duodenal types.

As previously mentioned, intestinal hemorrhage is the most constant symptom of an ulcer in Meckel's diverticulum. Usually the patient gives a history of previous massive intestinal hemorrhages followed by a period of months or years before recurrence. In a few instances only slight bloody or tarry stools are passed. The bloody stool may vary from bright red to black, although it is usually of a dark red color and may be fluid or partly clotted. The hemorrhage is not mixed with mucus, as in the dysenteries, nor does it have the raspberry jam appearance of intussusception. Collapse may result from a single massive hemorrhage, or a succession of lesser hemorrhages may reduce the patient within a few days or weeks to a state of extreme anemia. If the patient does not develop a perforation, he is likely to recover and then after a lapse of weeks, months, or years suffer a recurrence of the hemorrhages. This tendency to recurrence is a striking characteristic of this condition.

Next to hemorrhage the most frequent complication is perforation. When perforation occurs the symptoms and signs are those of a diffuse peritonitis, namely vomiting, abdominal pain, distention, collapse, generalized abdominal tenderness, and rigidity. Prior to perforation symptoms other than intestinal hemorrhage are generally lacking.

In the differential diagnosis the blood dyscrasias are easily eliminated. The bleeding time and clotting time are normal. The blood findings are those of secondary anemia. The cases of perforation present the picture of an acute surgical condition within the abdomen with an accompanying leukocytosis. An intussusception may be ruled out by the lack of obstructive signs, the lack of intense colic, the absence of a palpable mass, and the absence of mucus in the bloody stool. Bleeding duodenal or gastric ulcers are eliminated usually by the absence of epigastric digestive symptoms which respond to the effects of antacids and by a negative roentgenologic study. A Meckel's diverticulum can not ordinarily be demonstrated by x-ray examination. A rectal polyp may bleed profusely, but the history of tenesmus and examination with a proctoscope may prove the absence of this mass. Ruptured rectal varicosities may also cause sudden massive hemorrhage similar to the bleeding diverticula, but here again the proctoscope affords a means of differentiation.

Obviously the only treatment of Meckel's diverticulum is surgical.

Conclusions

1. A review of 9 cases of hemorrhage from the bowel due to Meckel's diverticulum has been presented.

2. Recurrent intestinal hemorrhage is the most constant symptom of peptic ulcer in Meckel's diverticulum.

3. This condition occurs most commonly before the age of 25 years, although no age group is immune.

4. The treatment is surgical.

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THE USE OF TELEVISION IN MEDICINE

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With the need for training thousands of men in radar and electronics, Captain William Eddy, Chief of Education for the Navy, realized that visual aids were necessary to cover the prescribed instruction in the time allotted him to prepare men for the Navy. He used every available visual aid to shorten the study periods and, without doubt, produced the greatest number of acceptable technicians ever trained in history. It was his interest in visual aids which stimulated the use of a special kaleidoscope for the correction of central visual defects and the improvement of vision in low grade myopia, thus aiding affected men in passing the required vision tests. In consultation on the use of television some four years ago, we both felt it was a readily usable adjunct in the field of surgery and have since been devising means of using it in teaching.

With the advent of a new camera recently constructed by R.C.A., it seemed feasible that a small portable unit could be constructed for use in the average operating room. For some time we have been working out the problem in the main studio of Paramount, the State Lake Building, Chicago, Illinois, with the assistance of Mr. Richard Shapiro and Mr. John Krimp, expert technicians for television. We worked with various types of lenses that would be necessary to televise the operations. In the home studios we used the long-focus narrow-angle lens; however, this lens was not available for the work at Cleveland Clinic, and we accordingly substituted one of the shorter focus lenses.

When the equipment arrived in Cleveland it was installed by Mr. Shapiro and Mr. Krimp. Several eye operations were televised, as were operations on the ear, neck, abdomen, and other parts of the body. It was felt that the black and white telephoto lens gave great contrast and detail and was entirely satisfactory for the operations about the head. With the use of longer focal lenses deeper cavities can be brought into view and the observer of the television screen sees the operation much more clearly and distinctly than does anyone else, including the first assistant; all save the operator himself are given a much better view than heretofore thought possible.

The apparatus was brought to Cleveland in the hope of learning the essentials for good observation of the procedures. We learned that with black and white, extreme illuminations are not essential. The ordinary operating room lights are sufficient, and the detail can be brought out by the proper lens in the camera. The operative area must be properly

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framed or placed in the field and care taken that it is not shifted out of position by injudicious movement of the patient. Care must also be taken by the operator to avoid projecting his hands or head into the field of the lens. With a variety of lenses of various focal lengths it is possible to show the general operative field and then to swing to the telephoto lens for detail. Recently we have tried out various types of filters which further enhance the contrast and bring out greater surgical detail.

In our experience we have been able to televise certain surgical procedures to a group of visiting clinicians, who were amazed at the clarity in the operative procedures. As the apparatus was combined with a loud speaker, a running commentary of the surgery could be given and all details of the operation were described. This in itself was a worth-while feature. We were fortunate in having the expert technicians under Captain Eddy's guidance so that our original attempts were not too amateurish. I am convinced that the surgical amphitheater is doomed and that, except for the occasional visitor in the operating room, the spectator will see more and be more at ease watching surgery on the television screen. He will see it better, larger, clearer, with better definition, and with more detail than heretofore thought possible.

Just a word of caution. The movements of the operator and assistants are magnified as much as the rest of the surgical procedure. It is well to remember that although the view of the surgery is enhanced tenfold, minute technical errors show up glaringly on the television screen; lack of ordinary technic, lack of proper use of the hands, sponging, suturing and the rest, all are magnified by contrast and detail. This is also true of the comments made at the time of operation. Statements made over the loud-speaker are received and coordinated with the surgical procedure, and care must be taken that they are accurate. It is now possible to record on the film the television image as it is also possible to record the speaking voice so that one can both televise and record operations by using this apparatus.

It is my belief that, because of its educational possibilities, there are no limits to the future of television. Its growth will be just as rapid as apparatus can be made available.

DENTAL FINDINGS IN HYPOPARATHYROIDISM IN RELATION TO PATIENT AND PROGENY

Report of a Case

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Hypoparathyroidism with decreased incretion of parathyroid hormone results in tetany, which is accompanied by a marked drop in serum calcium and a normal or elevated serum phosphorus. The tissues become depleted in calcium and develop neuromuscular irritability. In mild cases this may be evidenced by twitching, while in severe cases there are regular spasms of muscles with convulsions. The relationship of hypoparathyroid tetany to the teeth and oral structures has been the object of study and some animal laboratory experimentation by several investigators. Dental tissues, particularly dentine, are regarded as sensitive indicators in alteration of calcium metabolism.

As early as 1879 Magitot[1] postulated that hypoplasia of the enamel was associated with tetany. Fleischmann[2] in 1908 found parallel horizontal rows of bands superimposed around the teeth of children suffering from tetany. This was regarded as a type of enamel hypoplasia.

Erdheim[3] and Toyofuku[4] in 1911 made rat studies consisting of autotransplantation of parathyroid tissue, which produced changes in pulp, dentine, and enamel of the teeth. The greatest abnormality was found in the dentine. Gies and collaborators[5] in 1917 confirmed these findings in similar experiments on young rats, demonstrating that parathyroidectomy, without disturbance of the thyroid, resulted in deficient calcification of the teeth without producing effects on the general formation and dimension. Schour and coworkers[6] in 1937 found no retardation of eruption of the incisor teeth in albino rats. These workers demonstrated marked alteration of tooth substances appearing in the parathyroidectomized animals that survived for a long period. The alterations were particularly severe in those animals subjected to repeated pregnancy and lactation. Parathyroidectomized rats with a short period of survival, however, tended to show little change except an increase of density in the dentine. These changes occurred in the structures undergoing calcification at and following this operation. Tooth substance calcified prior to these operative procedures showed no alteration in structure. In these reports no reference has been made to the tooth structure of the progeny of the parathyroidectomized rats. There are

also no experimental data to illustrate the relation of pregnancy in hypoparathyroidism to dental pathology in humans.

In the case to be presented tetany existed over a period of twelve years, during which time the patient married and had four pregnancies, with all children living and well. The economic level of this family was low so that protein intake and fruits were either low or almost negligible. The patient stated that about once a month the children received an excess of candy.

Case Report

A woman, aged 25, came to the Clinic complaining of convulsions for a period of twelve years. She had been well until the age of 13, when at the onset of puberty she developed a large goiter. This was removed and was said to have weighed 1½ pounds. Six months after thyroidectomy the first convulsion occurred. For several years these convulsions averaged about one a month, always associated with menstrual periods. The patient married at the age of 17, and her first child was born one year later. The patient had no convulsions during pregnancy or lactation. The second child was born two years after marriage. This child never had cod liver oil or orange juice, with the diet consisting chiefly of cereals and vegetables. Four years after marriage a third child was born, and six years after marriage a fourth child.

The patient had been seen by several physicians in the period of twelve years, and a tentative diagnosis of epilepsy had been made.

Physical examination revealed blood pressure 105 systolic and 70 diastolic. Hearing was slightly diminished. Immature cataracts were present in both eyes. The thyroid showed an enlarged, nodular, firm right lobe. Trousseau's sign was positive in less than one minute. Chvostek's sign was also positive. Reflexes were sluggish. Blood calcium was 4.9 mg. per 100 cc., blood phosphorus 7.6 mg. per 100 cc. fasting.

Dental examination revealed all the teeth present except the six-year molars, lower left bicuspids, and the third molars. Dental caries was evident in several teeth. There was a total lack of oral hygiene, many teeth being covered with soft materia alba. No hypoplasia of the enamel was evident. The mucous membrane of the mouth was normal. The gingival tissues were slightly hypertrophic with some active inflammatory reaction and with slight suppuration on pressure. Soft tissue pockets were present interproximally,

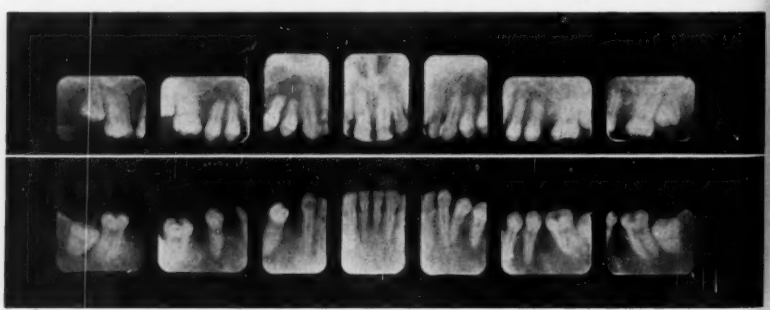

FIG. 1. Roentgenogram of teeth of patient.

but the teeth were not loose. Roentgenograms (fig. 1) revealed well formed teeth, the crowns of the posterior teeth having an unusually heavy cap of enamel. The roots of the upper bicuspid teeth were somewhat stunted. The alveolar bone appeared to be of normal density. There was little alveolar resorption around the teeth, although the teeth were traumatized by malocclusion. The cortical bone of the alveolar process (lamina dura) was sharp and distinct. The periodontal membrane space appeared of uniform, normal width. The third molars were unerupted but apparently had adequate space for eruption. They also had somewhat short roots. The D.M.F. quotient (decayed, missing, and filled) was 17.

The patient was placed under treatment, during which time the fifth child was born. Later, the teeth of all the children were examined. Roentgenogram studies were made of the teeth of two of these children. The eldest child, aged 10, showed marked malocclusion of the teeth of a class III type (Angle) prognathism. The teeth were, however, of normal shape, size, and color. There was no hypoplasia of the enamel. The gingival tissues were normal. The right bicuspids were in the process of eruption. The incisor teeth and the six-year molars had erupted. Six deciduous teeth were still present. No caries was noted in the teeth of the second dentition, although the molars presented occlusal pits of faulty calcification. A small carious lesion of the lower deciduous molar remaining was noted. The roentgenograms (fig. 2) of this patient revealed well formed teeth but somewhat smaller than average. Some teeth of the permanent dentition appeared congenitally absent. A developing upper cuspid, unerupted, presented a follicular type cystic development. The alveolar bone was of poor quality with weak traveculae, suggesting demineralization. The periodontal membrane was uniform but thin. The cortical bone margins of the alveolar bone (laminae dura) were not prominent. The dental age approximated that of the chronologic age.

The second child, aged 9, had considerable malocclusion of the teeth with a so-called end to end bite, suggestive of retrusion of the maxilla. The gingival tissues were normal. Twelve teeth of the second dentition were present, including the incisors and first molars. Eleven deciduous teeth were present, in six of which evidence of extensive dental caries was seen. The molar teeth of the second dentition showed deep pits of inadequate calcification in the occlusal surface. Through lack of cooperation, x-ray studies of this patient were not obtained.

In the third child, aged 7, the occlusion of the teeth was normal. The soft tissues were normal. Of eighteen deciduous teeth present, seven were carious. Four molars of

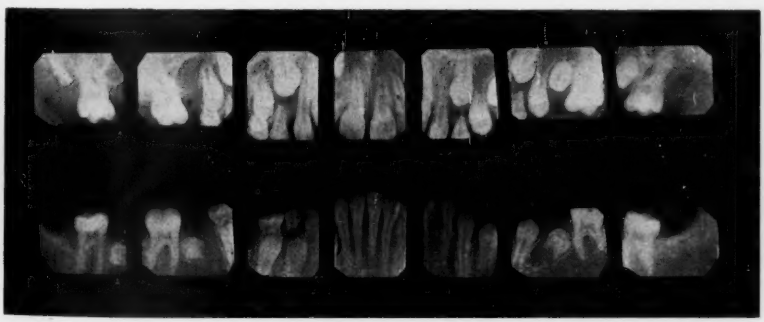

FIG. 2. Roentgenograms of teeth of child aged 10.

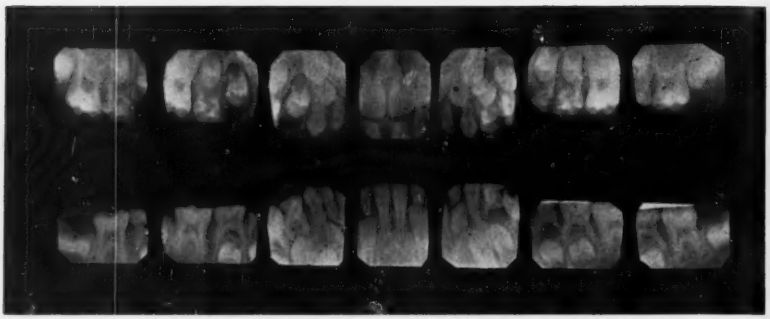

FIG. 3. Roentgenograms of teeth of child aged 7.

the second dentition, with the lower central incisors, were present and none of these were affected with dental caries. Roentgenograms (fig. 3) revealed badly carious deciduous molars, accompanied by dental sepsis. Well developed calcified posterior teeth were present, and there was no caries of the erupted six-year molars. In the upper incisors there was some sub-calcification of the dentine, as evidenced by indistinct pulp chambers. The enamel caps appeared thin and under-calcified. There was no clinical evidence of hypoplasia of the enamel of the teeth.

The fourth child, aged 5, had eighteen deciduous teeth, of which four showed caries. The lower six-year molars were erupted. The investing mucosa appeared normal. There was some malocclusion with an open bite anteriorly. Roentgenograms could not be obtained.

The fifth child, aged 22 months, was born after the patient had been under treatment for tetany throughout pregnancy. The child had sixteen deciduous teeth with no evidence of dental caries. The mouth, tissues, and occlusion of the teeth were normal.

Seven years after the patient was first seen roentgenograms of the lower arch were again obtained. In the meantime the patient had had the upper teeth removed. Unfortunately, there was no opportunity to study the extracted teeth histologically. However, a radiogram at this time revealed slight extension of the caries in three of the teeth, and in one a small new cavity was present. One lower tooth had been removed. The third molars had not erupted. No variation was detected in bone consistency other than could be explained by variation in x-ray technic. There was no evidence of alveolar resorption.

Summary

Clinical and roentgenographic findings on the dental structure of a patient with long-standing tetany, the result of hypoparathyroidism, has been presented. Studies are also presented of the five children, four of whom were born during the period of tetany symptoms. The anterior teeth of two children studied in roentgenograms revealed a suggestion of under-calcification with less dentine density and thin enamel caps. Three of the four children born during the period when the mother exhibited symptoms of tetany demonstrated malocclusion. Two of these four children had some evidence of prognathism of the mandibles

or suggestion of maxillary underdevelopment. This might also be said of the third child, who exhibited an open bite anteriorly. Dental caries was marked in the deciduous teeth of three of the children born during the period of tetany. This included the child whose occlusion was normal. The erupted teeth of the second dentition showed developmental occlusal pit defects but no caries. The eruption of the teeth was consistent with the chronologic age of the children. Anodontia was present only in the eldest child. Without fruit juices and vitamins supplementing the diet, in no instance did the gingival tissues of the patient or children show a striking deficiency state.

While under treatment, which included a diet list of high calcium and low phosphorus content, the patient had her fifth child. Dental examination of this child at the age of 22 months demonstrated no caries. All the deciduous teeth were present except the second deciduous molars, whose eruption occurs usually between 2 and 2½ years.[7] Occlusion was normal.

Conclusions

In a patient with long-standing tetany accompanied by very poor dietary regime and oral neglect, the caries index was not significantly greater than average. Mann *et al.*,[8] in a recent report on the activity of dental caries in malnutrition and in well nourished patients, noted that the D.M.F. quotient (decayed, missing, and filled) of the experimental malnourished group average was 4.54 as compared to the control group average of 14.94 Our patient exhibited a D.M.F. quotient of 17. Possibly dietary deficiency may have controlled caries sensitivity in this case. I prefer to believe, however, that hypoparathyroidism had no effect upon the calcium metabolism of the developed tooth, and, inasmuch as the teeth were well developed and calcified prior to the onset of tetany symptoms, no structural defects resulted from this condition, which can be considered predisposing toward dental caries in an adverse environment. The children born during the period of tetany, however, readily developed caries of the deciduous teeth, causing their early loss. This, in turn, resulted in the malocclusion of the teeth with altered jaw development. The finding that the third child had normal occlusion supports this view. The retention of the carious deciduous teeth in this child would account for the maintenance of proper space for developing teeth of the second dentition, inhibiting the tendency toward altered jaw development. The malocclusion in the fourth child appears to be congenital, possibly pernicious habits such as thumbsucking being contributory; this was not brought out in the history. The low incidence of caries in the child is difficult to explain. The ano-

dontia of the oldest child may be related to the endocrine dyscrasia of the mother. This condition, however, may be associated with genetic variation, and as it does not involve any of the other three children but follows the Mendelian pattern, I believe that heredity rather than congenital endocrine factors should be considered primary. The period of eruption of the teeth was not disturbed, as has been pointed out by other investigators. Hypoplasia of the enamel of the teeth in either the deciduous or second dentition was not found. This does not agree with statements of early investigators. There was roentgenographic evidence of impaired calcification of upper incisor teeth of the second dentition (which completes coronal development prior to birth) and of the deciduous teeth whose calcification begins about the fourth month *in utero*. Although marked caries susceptibility appeared to be present in the deciduous teeth of the children, it could not be described as widespread or rampant, and the fact that the teeth of the second dentition showed little evidence of caries suggests some protective factor[9,10] modifying the effects of structural defects, an inadequate diet, possibly excessive sugar intake, and poor oral hygiene habits. Although the diet as described by the patient appeared to be substandard, clinically no deficiency state could actually be considered as affecting the soft investing tissues of the mouth of the patient and children.

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MECHANISM OF DEMYELINATING DISEASES OF THE CENTRAL NERVOUS SYSTEM

A Therapeutic Approach with Anticoagulants

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Ten years after Arthus[1] presented the histopathology of a local anaphylactic reaction in the skin of sensitized animals, Rachmanow[2] described degenerative alterations in the neurone cells of animals that had died in anaphylactic shock. That the Arthus phenomenon could be produced in the brain was demonstrated when rabbits sensitized to horse serum were shocked by intracerebral injection of that antigen. The site of the injection became one of violent pathology, for hemorrhages, thrombi, necrosis, scavenger cells, and microglial and oligodendroglial infiltrations were demonstrated.[3]

Experimental cerebral anaphylaxis in monkeys produced neuropathologic changes comprising two types of lesions.[4] The first was at the site of injection of the shocking dose of antigen and was similar to that described above. The second type of lesion was that of a disseminated encephalopathy in which the areas of demyelination were perivascular. The microscopic picture of these dispersed lesions revealed (1) perivascular infiltration by a variety of cellular elements; (2) axis cylinder destruction; (3) occlusion of small blood vessels by thrombi and endarteritic processes, and (4) intra and perivascular edema. Chronicity of the condition and protracted sensitization with the antigen were reflected in a change in the nature of the perivascular reaction. The change in reaction was from that of an acute hemorrhagic type associated with an exudate of polymorphonuclear leukocytes to the more chronic picture involving lymphocytes and finally granulomas and giant cells.

Basically the similarities and identities between the pathology of experimental cerebral allergy and the pathology of demyelinating diseases such as multiple sclerosis are these:[5]

1. The demyelinating process is chiefly perivascular in both conditions.
2. Hemorrhages are a major finding in the acute processes, while a paucity of hemorrhages characterizes the chronic stages of each.
3. Degeneration and necrosis of blood vessel walls are common to both.

4. Thrombus formation is seen in the acute stage of a demyelinating disease, while experimental anaphylaxis involving any tissue includes all stages of thrombus formation in the pathologic picture.

5. The perivascular reaction is predominantly perivenous, although it may involve arteries and capillaries.

6. Necrosis is a frequent feature of both processes.

7. In general, the patchy or diffuse gliosis of the demyelinating process is viewed as the equivalent of the scar tissue repair in other organs. Patchy gliosis has been reported in the later stages of experimental cerebral anaphylaxis.

The greatest disagreement among neuropathologists seems to arise from the etiology of the demyelinating process. Ferraro[5] has presented his argument based on the analogy of the cerebral pathology of demyelinating diseases and that of cerebral anaphylaxis. With this approach he hopes to open new avenues of investigation. Putnam[6] has introduced a different theory based on a peculiar disturbance in the clotting mechanism of the blood of patients suffering from multiple sclerosis. There is experimental evidence to show that demyelinating lesions can be produced through retrograde obstruction of cerebral venules, and thrombi, among other changes, are regularly seen in the acute lesions of multiple sclerosis in man.[7, 8] Thrombi have also been noted in other body organs in acute or progressive cases where encephalomyelitic changes were taking place.[9] Putnam has summed up his theory as follows: "There are individuals who suffer from a peculiar lability of the clotting mechanism of the blood. Whether this is congenital or acquired is not clear. If it exists, however, any slight disturbance of the equilibrium of the body may precipitate a shower of minute thrombi in various tissues. Most of these cause no permanent damage, but any that occur in the brain leave a permanent landmark behind and a local vascular abnormality which predisposes to further clotting. If the process is sufficiently stormy, a widespread destruction is produced, and the patient dies with the manifestations of 'encephalomyelitis'."[6]

Irrespective of the cause, it is generally agreed that each sclerotic plaque of multiple sclerosis goes through an acute state. It is in these acute lesions that thrombi are most frequently seen. Putnam reasoned that any gain from specific treatment must be directed toward preventing relapses and that this might best be done through depressing the ability of the blood to form thrombi. Thus he turned to the use of anticoagulants, and his group has recently reported a series of multiple sclerosis

cases that were continuously treated with the anticoagulant, dicoumarin, over a long period of time.[10]

The origin of plaques through thrombus formation does not necessarily eliminate the explanation of the pathologic picture of demyelinating diseases as a part of an allergic reaction. The formation of thrombi may be only a step in the march of events in the pathologic parade. The consistent production of thrombi in cerebral anaphylaxis has been pointed out by many workers, as previously mentioned. Putnam suggested that the instability of the clotting mechanism might be one aspect of allergy.[9] During an allergic reaction damage may occur to blood vessel walls in the form of periarteritis, or intimal changes may be induced which in turn would encourage thrombus formation in such vessels. It is possible, too, that vessels may be compressed by perivascular edema resulting from an allergic reaction, thereby indirectly causing thrombi to form in them.[11] An unexplained thin sheathing of the retinal venules in a group of 34 patients has been reported by Rucker.[12] This vessel abnormality was especially noticeable toward the periphery of the ocular fundi. Twenty-one of these patients were subsequently diagnosed as having multiple sclerosis, while 7 others were suspected of having a related disorder. Spasms of fundus arterioles have been observed directly with the Morton ophthalmoscope in cases of multiple sclerosis. These spasms were accompanied by the subjective visual impairments of shimmering and scotomata.[13]

Once the initial pathologic process has been established, the relapsing nature of this group of diseases may well be the result of subsequent, specific, antigen-antibody reactions for which the brain and cord are the shock organs. Kennedy[11] states that many things about multiple sclerosis suggest paroxysms of localized allergic edemas. Among these are the episodic character with intermissions, curability of the acute crises, and attacks on the optic nerve.

The administration of anticoagulants in the treatment of multiple sclerosis, whether it be based on Putnam's theory or on the Ferraro concept of cerebral allergy, is directed against the formation of thrombi. Such treatment is justified since thrombus formation is one of the links in the chain of events leading to demyelination, and preventing their formation offers a logical attack against the progress of the pathologic process. On this basis the information accumulated in the treatment of 12 cases of multiple sclerosis using the anticoagulant, dicumarol, (3, 3′–methylenebis [4-hydroxycoumarin]) deserves passing review.

All patients were hospitalized and a prothrombin time determined before dicumarol was given. The Quick method of determining the prothrombin time was used throughout this series. All dicumarol was

given orally. Treatment was inaugurated by a dose of 300 mg. the first day and 150 mg. the second day. A prothrombin time was determined on the third day and the succeeding dose governed by the effect of the drug given thus far. After the first three days a maintenance dose ranging between 50 to 100 mg. every other day was found to be sufficient to maintain the prothrombin time at the desired level of 50 per cent of normal (normal = fifteen seconds). It was essential to do prothrombin time determinations at least two or three times weekly until the maintenance dose of dicumarol became established. Later in a few cases this procedure was reduced to once a week, especially when the maintenance dose of dicumarol required to keep the prothrombin time at the desired level became fairly constant. It was deemed wise to keep the patients under close hospital observation for the first two weeks of treatment, during which time a safe plan for continuing the drug over a long period of time could be determined. An attempt was made to keep the prothrombin time as close as possible to 50 per cent of normal for the duration of the treatment.

Of the 12 patients treated by this method, 7 were women (58.3 per cent) and 5 were men (41.7 per cent). The average age of patients at the start of treatment was 34 years. The oldest was 55 years and the youngest 23. In the average case, the disease had been in progress forty-six months before being treated with dicumarol. One patient had had symptoms attributed to the disease for sixteen years prior to treatment.

Six patients (50 per cent) gave a personal or family history of allergy. Three such histories are related below.

Case 1. A white woman, aged 35, had had recurrent bouts of hives all her life. She was found to be sensitive to rayon and wool. Questioning revealed that she had had asthma and hay fever in 1935. The patient was skin tested for undulant fever in 1945 and gave a markedly positive reaction to this test. A course of undulant fever vaccine therapy had to be discontinued because of the violence of reaction. A year later another attempt was made to give her graduated doses of brucellin, but because of the untoward reaction with high fever this treatment had to be stopped. This patient believed she had had her most crippling relapse of multiple sclerosis after the fourth injection of brucellin. This case has been diagnosed elsewhere by a very competent neurologist as an allergic encephalomyelopathy. He has prescribed an autogenous vaccine made from sinus washings and tonsil swabbings. The patient has been on a desensitizing program for several months using this vaccine. One communication from the patient (January, 1947) revealed subjective improvement.

Case 2. A beauty shop operator, aged 32, had had a rather severe contact dermatitis on her hands when she presented herself for dicumarol therapy. Patch tests revealed that she was very sensitive to tobacco and to two hair waving lotions which she was using in her daily work.

Case 3. A white woman, aged 38, on whom the diagnosis of multiple sclerosis was made, revealed that she had had hives for the first time in August, 1945. The urticaria appeared intermittently throughout the following summer until November, 1946. The responsible allergen or allergens were not known. The patient stated that while the hives were at their height of severity she suffered a marked exacerbation of the symptoms which were characteristic of multiple sclerosis.

With cooperation of the department of allergy a series of patients suffering from multiple sclerosis and its related disorders is being skin tested. Stock mixed respiratory vaccine, stock mixed stool vaccine, and individually tested common bacterial invaders are the antigens being used. It is hoped that some information can be gathered with which a desensitizing program can be worked out for selected cases. A report of this work will appear at a later time.

The average length of treatment was forty-two days, the shortest being a fourteen-day period and the longest a one hundred fifty-day period at the time of this report. In this study any one of the three following reasons was considered sufficient for stopping the treatment: complications from hemorrhage, especially into the kidney; inability to establish a safe program for administering dicumarol during the two-week hospitalization period, and instances where it was impossible to check the patient's prothrombin time regularly after he left the hospital. At present 8 (66⅔ per cent) of the patients are still on treatment. Several more patients have been added to the series since this report was written.

Ten of the patients (83⅓ per cent) expressed subjective improvement. This has been noted as early as seven days after treatment was started. Improvement in vision is one of the first things the patient will proffer. Expressions, such as, "My hands do not tingle so much," "I'm steadier on my feet," or "I feel that I can walk better" are frequently heard. These may only be unbased enthusiasms released from persons who, in their mind's eye, had already consigned themselves to life in a wheel chair.

Unfortunately, objective evidence of improvement is not so prevalent. Two patients (16⅔ per cent) showed evidence of objective improvement. The most striking change was noted in a 29-year-old white woman who could not urinate spontaneously and had required daily catheterizations by her family physician prior to coming to the hospital. During the second week of dicumarol treatment she was able to void spontaneously and has had no difficulty in this respect since.

In another patient, a 30-year-old white woman, the bilaterally positive Hoffman sign and sustained ankle clonus were changed to unilateral findings.

Conclusions

It is concluded that the results of dicumarol treatment of multiple sclerosis have been indifferent to slightly encouraging in a small series of cases. More information concerning the value of this method of treatment is becoming apparent as prolonged therapy continues in most of these patients and in additional patients with the diagnosis of multiple sclerosis.

A quick review of this small sampling should serve to evoke further interest in the use of anticoagulants in the treatment of multiple sclerosis, and, what is equally important, should stimulate a continued interest in the role of allergy in this stubbornly mysterious demyelinizing process.

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INDUCED HYPOTENSION IN THE CONTROL OF BLEEDING DURING THE FENESTRATION OPERATION

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Induced hypotension for the control of bleeding during operation, as first described by Gardner,[1] has proved a new and valuable aid for the control of less severe but troublesome bleeding during delicate and confining types of operative procedure such as the fenestration operation.

In approximately 30 per cent of the cases submitted to the Lempert fenestration operation there is troublesome bleeding. This bleeding reduces the speed of the operator, and, because of the effort in removing the blood by irrigation and suction, added trauma is induced in the vicinity of delicate structures such as the ear drum, tympano-meatal flap, and the seventh nerve.

More important, however, is the complete control of bleeding during the preparation of the fenestra. A bloodless field is desirable, as any blood entering the fenestra must be removed from the perilymphatic space within the bony labyrinth. This removal increases the amount of trauma to the membranous labyrinth, and many times it is impossible to remove all of the visible blood even with irrigation and suction.

It therefore becomes obvious that any method of effective control of this bleeding is desirable.

The procedure of controlled induced hypotension has been used in 24 patients undergoing the fenestration operation. In all of these cases the troublesome bleeding encountered during the preparation of the tympano-meatal flap and the construction of the new fenestra has been satisfactorily controlled. The frequency and severity of postoperative labyrinthitis has been reduced, probably due to reduction of the amount of blood entering the fenestra and also less trauma to the membranous labyrinth. Postoperative labyrinthitis usually occurs in patients having increased tendency to bleeding during operation. We therefore believe that the control of bleeding during preparation of the flap and construction of the fenestra contributes to a better hearing result.

Experimental Findings

Kohlstaedt and Page,[2] in experiments with dogs in 1943, described an ingenious method for the study of shock by arterial bleeding and infusion. Briefly, this method consists in placing a cannula in the femoral artery directed toward the heart. This cannula leads to a closed reservoir into which the dog is bled until the blood pressure is lowered to 30 mm. Hg. The blood is mixed with an anticoagulant during its withdrawal. The arterial pressure is recorded on a kymograph. To raise the blood pressure the blood is infused into the femoral artery by increasing the pressure in the closed reservoir by pumping air into it. This method permits the investigator to reduce the blood pressure to any desired level, hold it there as long as desired, and then bring it back by infusion of the removed blood. In the treatment of hemorrhagic shock these authors found intra-arterial infusion more effective than the intravenous method.

Method

The management of controlled induced hypotension is carried out by the department of anesthesia. The bloodletting is begun at a time selected by the surgeon so that the maximum effect will be obtained during the preparation of the tympano-meatal flap and the creation of the fenestra.

The radial artery is exposed through a longitudinal incision medial to the styloid process of the radius after establishing the presence of a functioning ulnar artery. In the lumen of the artery is secured a two-limbed glass cannula, its tip directed toward the heart. One limb of the cannula is connected by rubber tubing to a vessel containing 50 cc. of 4 per cent citrate solution. The other limb leads to a supply of heparin 0.01 per cent solution, a manometer for registering direct arterial pressure, and a vessel for returning the blood under pressure after filtration. As the apparatus is assembled the tubing, cannulas, and connectors are filled with the heparin solution. At intervals during the time that the apparatus is in use, 5 cc. quantities of the heparin solution are injected into the cannula in order to prevent the formation of a clot within it.

The arterial blood is allowed to flow into the collecting bottles (500 cc. into each) until the blood pressure falls to 80 mm. Hg or until the operative bleeding is satisfactorily controlled. The quantity of blood which it is necessary to withdraw has varied in the present series from 1000 to 3100 cc. During the time that this quantity of blood is outside the body it is essential that the patient be watched with the greatest care in order that the blood pressure may be supported at once, if needed, by the arterial reinfusion of blood.

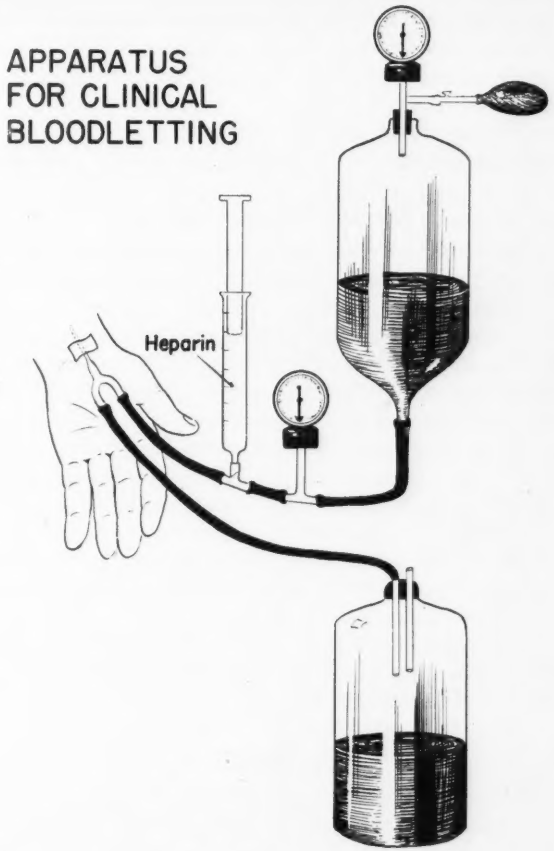

FIGURE. Lower limb of cannula leads to receptacle for collection of blood which is filtered before being returned to patient. Upper limb connects to a heparin supply, arterial pressure manometer, and vessel fitted with pump to control pressure for returning the blood to patient.

At the termination of the period when controlled hypotension is needed, the blood is returned to the patient by the arterial route. Ordinarily the last pint is withheld as the blood volume tends to approach its normal value by the passage of tissue fluids into the vessels. This withheld pint may be returned to the patient during the subsequent twenty-four hours or may not be used at all, affording a mild dehydration effect which, it is believed, reduces postoperative headache and vertigo.

After the fenestra has been completed the tympano-meatal flap is held in place over the fenestra by parresined lace-mesh gauze, and the mastoid cavity is snugly packed with pledgets of sulfathiazole-impregnated vaseline gauze. This packing of the bony cavity is sufficient to prevent recurrence of bleeding after the operation has been completed and the blood pressure has been restored to normal. (Figure)

Precautionary Measures

Controlled induced hypotension is a procedure which should be carried out only by a competent physician. The following precautionary measures deserve special mention:

1. A careful aseptic clot-free technic must be employed throughout.
2. Short "stabilizing periods" during the bloodletting give an accurate estimate of the adaptability of the cardiovascular system.
3. Constant check on the blood pressure during the hypotensive period is essential to avoid sudden serious collapse.
4. The amount of blood withdrawn varies with different patients, but in none should it be rapid and uninterrupted to a previously estimated total amount.
5. The blood (with the exception of a half-liter) should be reinfused before removal of the arterial cannula and before the patient is moved from the operating table.

In the series represented in this article, in which the above precautions were observed, no untoward after-effects or complications have followed the use of this procedure.

Comment

Controlled induced hypotension has been found a very effective and safe procedure in the control of troublesome bleeding during the most difficult and important phases of the fenestration operation. The operating time has also been shortened in these difficult cases.

The incidence of postoperative labyrinthitis has been markedly reduced, and the amount of decibel gain in hearing is, therefore, greater.

The procedure is not advocated for all fenestration cases but should be reserved for those that show a tendency to bleed. If carried out under proper precautions we believe it to be a safe and valuable adjunct in fenestration surgery.

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INITIAL TREATMENT OF BURNS OF THE HAND

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In treatment of burns of the hand, as in treatment of any injury to the hand, the physician must preserve all tissue possible and institute a type of treatment which will permit prompt healing of the wound and early restoration of function. The doctor who first sees and treats a burned hand is given an opportunity never again afforded either to him or to any doctor who may subsequently treat the case. If the burned hand is seen within six or seven hours after injury it is still possible to convert the burned area into a clean wound and prevent sepsis, which will certainly intervene if the wound is left exposed. It is this sepsis which frequently does much more damage to the tendons and small joints of the fingers than the burn itself.

Since the original treatment of a severely burned hand is so important, every physician should know how to apply a satisfactory dressing. If the initial treatment has been adequate, the surgeon to whom the patient is referred for subsequent treatment is not confronted with the problem of a hand stiffened by sepsis which has been permitted to develop because of an unsatisfactory initial dressing.

First and second degree burns of the hand do not present a serious problem because the epithelial covering of the hand has not been entirely destroyed. Almost any type of treatment will result in adequate healing provided, of course, infection is kept at a minimum. In an extensive burn of the hand, however, it frequently is impossible to ascertain at once whether the burn is confined to the skin or whether it has extended to the subcutaneous structures. It is with such cases that we are chiefly concerned in this discussion.

Of primary importance is the general care of the patient. The administration of parenteral fluids, blood, and plasma may be necessary to combat shock. It must also be remembered that the hand is a very sensitive part of the body, and patients will require considerable sedation for relief of pain. It is folly to attempt any local treatment of the burn without adequate sedation, and, whenever possible, general anesthesia should be employed. An intravenous anesthetic of sodium pentothal is especially effective, although any type of general anesthetic may be used.

The hand is thoroughly but gently cleansed with soap and water, using gauze sponges or a brush on the unburned areas and cotton pledgets on the burned areas. Blebs need not be broken. Care must be taken not to remove or damage any skin which may possibly retain any

degree of viability. No attempt should be made at this time to determine the depth of the burn. Even though it may seem apparent that amputation of one or more fingers is inevitable, such amputation should be delayed at this time. Needless to say, all rules of surgical aseptic technic should be strictly followed.

After spending at least fifteen or twenty minutes in thorough cleansing of the injured hand, wrist, and forearm, the surgeon changes his gown and gloves, drapes the extremity with sterile sheets, and then applies a large pressure dressing. The area is first covered with a layer of greased gauze. Simple vaseline gauze may be used, or gauze impregnated with boric acid ointment, penicillin ointment, or any other type of bland antiseptic ointment. It is imperative that the greased gauze be smoothly applied. Four or five layers of plain gauze dressings are then applied. This is followed by a large amount of mechanic's waste, extending from finger tips to the elbow (fig. 1b). This waste

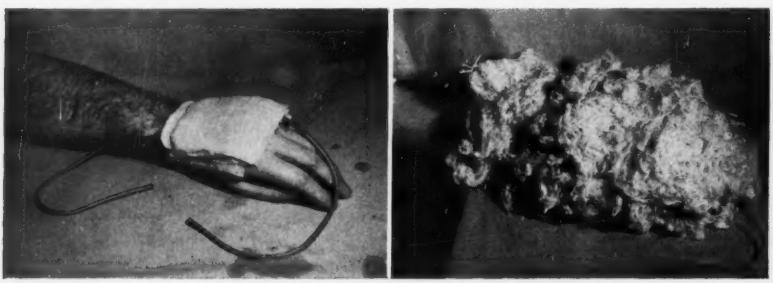

FIG. 1. (a) The granulating burned area on the dorsum of the hand has been covered with strips of fine mesh gauze moistened with sterile saline. Two rubber catheters have been incorporated in the moistened gauze dressings which have been placed over the bandage gauze strips. (b) Fluffed up mechanic's waste has been placed over the gauze dressing completely covering the hand and forearm.

must be fluffed up by hand before it is applied because it has a tendency to mat down when sterilized. A few abdominal cotton pads are then placed over the mechanic's waste and the entire dressing snugly compressed with an elastic bandage. If elastic bandages are not available, a continuous strip of stockinet which has been cut on the bias will serve just as well. A simple gauze bandage may be used but is not as effective in maintaining a constant even pressure. A plaster slab is incorporated in the outermost turns of the elastic bandage (fig. 2a). This splint is placed on the volar aspect of hand and forearm to keep the wrist in extension and provide more stability to the dressing. If it is desired to save the elastic bandages, they may be covered with a layer

of roller bandage gauze prior to application of the plaster slab, and the plaster slab may in turn be held in place by the roller bandage. This will prevent the plaster from adhering to the elastic bandages.

In applying the pressure dressing, care must be taken to place the hand in a position of function, that is, all joints of the fingers partially flexed and the thumb rotated into a position of opposition. It is especially important to see that the metacarpophalangeal joints are all flexed about 40 degrees, since these joints are prone to become stiff in extension. All too frequently one encounters a badly burned hand which has been treated for several weeks on a board splint; all joints of the fingers have become stiff in extension, and the thumb is fixed by the side of the hand in the plane of the palm. Such a hand will require many weeks of occupational and physical therapy to displace the thumb from the plane of the palm and to obtain sufficient flexion of fingers for any useful function.

After the pressure dressing has been applied it is often advisable to suspend the arm to prevent undue swelling. Elevation of the hand on a pillow may frequently suffice, but by suspending the arm one is assured that it will remain elevated day and night. A pad is placed over the humeral condyles, and, with the elbow flexed a few degrees beyond a right angle, a long strip of 3-inch adhesive tape is fastened along one side of the pressure bandage on the forearm, then around the elbow and up the opposite side of the forearm. The two ends of the tape are fixed to a block of wood to which a rope is attached; this rope may be passed through a pulley and sufficient weight applied to keep the arm suspended, or the rope may simply be tied to an overhead bar on the bed (fig. 2b).

If the pressure dressing, including plaster reinforcement, extends above the elbow, one will encounter no difficulty in applying suspension straps. When the dressing includes only the hand and forearm, however, it may be necessary to secure the adhesive suspension strap with two additional strips of adhesive along the medial and lateral aspects of the upper arm. If suspension straps are not passed beneath the flexed elbow there is a tendency to pull off the pressure dressing when the arm is suspended.

When the first dry pressure dressing is removed after seven to ten days, it is advisable to change the dressing in the operating room so that any necessary debridement and skin grafting may be done while the wound is still relatively clean. It is imperative that all denuded surfaces be covered promptly with skin. Bones and tendons which are left exposed to the air will certainly undergo ischemic necrosis, and it

is frequently possible to prevent many months of disability by prompt covering of exposed surfaces with skin.

If sufficient time has elapsed to assume that thorough cleansing of the burned hand will not produce a relatively aseptic wound, a moist pressure dressing must be applied. This type of dressing is completed exactly as described above but with the following modifications: strips of fine-meshed bandage gauze are moistened with sterile saline or boric solution and applied smoothly over the wound; three or four layers of regular gauze dressing, also moistened with saline or boric solution, are then applied. Over these are laid one or more soft rubber catheters with multiple holes cut along the distal two or three inches of the catheters. Another three or four layers of wet gauze dressings are then applied over the catheters (fig. 1a), and the dressing is finally completed with

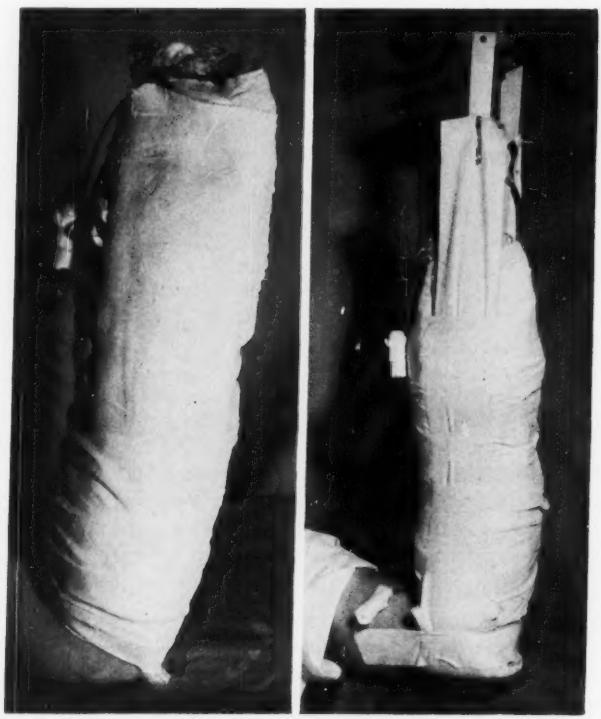

FIG. 2. (a) The moist pressure dressing has been completed with abdominal cotton pads and Ace bandages, and a plaster slab has been incorporated with roller bandage to keep the wrist in extension. (b) Strips of adhesive have been applied to suspend the arm.

mechanic's waste and cotton pads as described above. The open ends of the catheters are left outside the dressings and are sealed with a sterile glass plug or covered with a sterile dressing (fig. 2a). Into these catheters may be instilled sufficient sterile saline or sterile boric solution to keep the inner gauze dressing moist. The exact amount of solution to be instilled can be learned only by experience, but it is always better to keep the dressings too moist than too dry.

A moist pressure dressing of this type is of great value in cleansing septic granulating wounds prior to skin grafting, and the same type of dressing is re-applied when a free skin graft has been placed on the granulating surface. Pyocyaneus infection is frequently encountered in these chronic granulating wounds, and presence of this organism will almost surely prevent adequate "take" of a split-thickness skin graft. If such an infection is present it is well to keep the pressure dressing moist with ½ per cent acetic acid solution for a day or two both before and after the skin graft has been applied. These moist pressure dressings are usually changed every day or two. They may be left in place for five or six days if desired, although this is seldom indicated except with a split-thickness graft.

Development of excessive scar tissue in the hand and contracture of small joints in the fingers are kept at a minimum, and rehabilitation of the burned hand is greatly facilitated by employing the principles of treatment outlined above. There is nothing new or original about this type of pressure dressing, but it is hoped that further emphasis on this method will facilitate its adoption by all physicians who are called upon to treat a severely burned hand.

PSYCHOSES ASSOCIATED WITH VASCULAR DISEASE

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Theoretically, senility and arteriosclerotic brain disease are distinguishable, but in practice such a differentiation often becomes difficult.

In reviewing the early literature on mental symptoms of the aged, one discovers that much has been written concerning senile psychoses, but material on the psychoses of arteriosclerosis is scant.

The arteriosclerotic brain and the senile brain each have distinct pathologic patterns. Disease of the blood vessels is not constant in the aged and in itself cannot be considered the sole basis for the pathologic findings of senility.

In general, arteriosclerotic brain disease occurs in people over 50 years of age. The fact that there is a familial variation of this disorder has been well established. Certain factors such as worry, alcoholism, extreme mental exertion, and diet are considered to be contributory. The condition of the "arterial tree" is often an excellent index of one's age, and the adage that "a man is as old as his arteries" holds much truth.

Cobb classifies the pathologic changes of cerebral arteriosclerosis as follows:[1]

1. Large vessel sclerosis. This type involves primarily the arteries of the base of the brain as well as the larger vessels of the cerebrum, cerebellum, brain stem, and choroid plexus. The process is rare in the vessels of the cortex, and from the histologic standpoint resembles arteriosclerosis as seen throughout the entire vascular system.

2. Arteriolarsclerosis. Arteriolarsclerosis is characterized by a hyaline degeneration of the intima in the arterioles and capillaries. It is a diffuse hyperplastic process involving primarily the vessels that supply the cerebral cortex and nuclei. In advanced cases degeneration is also seen in the media and adventitia. This type is commonly associated with hypertension.

3. Capillary fibrosis. Capillary fibrosis is most frequently seen in presenile dementia and Alzheimer's disease. In this type of pathologic change, thickening of the adventitia of the capillaries is observed. Cobb states that this process may be the result of arteriosclerosis rather than part of the arteriosclerosis itself.

4. Endarteritis. Endarteritis resembles the changes seen in syphilis and is rarely encountered in arteriosclerosis.

5. Vessel calcification. Calcification of cerebral vessels occurs in late stages following fatty degeneration of the intima.

Subsequent remarks regarding cerebral arteriosclerosis shall be confined to the clinical pictures observed in two types of vessel involvement, namely, the disorders of essential hypertension or arteriolarsclerosis and those encountered in simple arteriosclerosis or large vessel sclerosis.

The patient afflicted with arteriolarsclerosis may be relatively young, that is, in the third to fifth decades of life. The clinical picture is usually characterized by excessive and persistent elevation of both the systolic and diastolic blood pressure, moderate reduction of renal function, impairment of the heart from hypertensive disease and varying degrees of petechial hemorrhage, softening and scarring of the brain.

There has been much controversy as to whether disease of the blood vessels causes hypertension or whether the reverse be true. Regardless of cause and effect, it appears rather certain that emotional strain may predispose to or cause disease of the blood vessels. The relationship was well illustrated by Kasanin in a paper entitled *Early Psychic Invalidism*[2] in which he described mental involvement in young people who were subjected to the rigors of the world war and Russian revolution. These individuals presented clinical and pathologic evidence of cerebral arteriosclerosis.

The pathology of arteriolarsclerosis of the central nervous system may readily simulate the condition found in the kidney of essential hypertension, characterized by petechial hemorrhages, loss of cells, and resultant fibrosis. Because of multiple petechial hemorrhages having been present in the brain, the amount of resultant scarring may be pronounced. This scarring gives rise to extensive loss of cortical cells and defects in the white matter.

Mental symptoms of essential hypertension are extremely variable, depending upon the degree of involvement. Headache, vertigo, head noises, tension, and anxiety are common. Irritability, outbursts of impulsive behavior, and emotional instability characterized by unprovoked laughing or crying are frequently observed. Intelligence may be unimpaired in the early stages. Fluctuations of the above symptoms are noted from time to time even though the basic disease continues to progress.

Providing death does not intervene, the mental changes tend to become chronic. In addition to the above findings, impairment of memory becomes evident, the power of concentration is lessened, endurance and

initiative are diminished. The prognosis in this condition is uniformly poor, and the process may run a course of a few months or years. On rare occasions such individuals develop delirium, manifest amentia, and actually may be reduced to a vegetative level.

The treatment of this mental illness is quite limited and, unfortunately, is not too successful. As soon as the condition is suspected the patient and relatives should be advised as to the general hygienic measures indicated, warned regarding the patient's participation in undue physical and mental exertion, and his avoidance of emotional strain or tension. In the earlier phases treatment may be carried on in the home, but as the disease progresses and the mental status becomes uncertain, hospitalization in a sanitarium or mental hospital is advisable.

All measures to reduce blood pressure should be employed, and, unless the condition has progressed too far, sympathectomy should be given serious consideration. It is possible that reduction of the blood pressure may retard or completely arrest the arteriolar involvement of the brain.

A note of caution about the use of certain medical words and conversation before a patient might not be amiss. This applies particularly in discussion of arteriosclerosis and hypertension, for the anxiety of the hypertensive or arteriosclerotic patient has often been increased by injudicious use of these terms. The average person is sufficiently well versed in medical terminology to be aware of the fact that these two terms have an ominous connotation. Instead, why not use the phrase, "arterial changes of aging", or in the case of the hypertensive say, "I am satisfied with the test", or "the blood pressure is satisfactory". These phrases have been suggested by Thewlis in his recent book, *The Care of the Aged*.[3] He states, "There is no type of patient in whom exaggerated fears are more evident than in hypertensive victims, and one should not add insult to injury by a careless selection of words. These patients weigh every word the physician utters. Therefore, the wise physician weighs his words at every turn, and never deviates from his formula."

Cerebral arteriosclerosis of the simple or large vessel type occurs for the most part in people over 50 years of age, and some investigators consider it to be a normal physiologic process in persons over that age.

"Wartman found that 90% of men, and 85% of women past sixty, had marked cerebral arteriosclerosis; all others had some pathologic condition of the brain at the time of death, yet they did not present marked symptoms."[1]

Disorders of personality arising on the basis of arteriosclerotic brain disease accounted for approximately one-third of the organic reaction types in Billings' series of cases.[4] The onset of mental symptoms in this

type of sclerotic vessel change may be gradual or may follow an apoplectic seizure of minor or major severity. The degree and extent of vessel involvement governs to a large measure the mental symptoms and neurologic picture encountered. In the less complicated cases, headache, dizziness, insomnia, and minor personality changes may be present. Mental depression and paranoid trends often present themselves as added features. Persons having mild to severe vessel involvement demonstrate defects of memory of recent events, and the amnesia often increases to include remote happenings. Occasionally confabulation is resorted to in filling memory gaps. Emotional instability giving rise to pathologic laughing or crying is not uncommon. Defects in judgment, impairment of mental concentration, and easy mental fatigue are common. As a general rule, until more advanced stages are reached the basic personality is not markedly altered. However, as the disease progresses the once amiable person may become irritable and manifest impulsive behavior. He may further reveal indifference in his personal appearance, whereas previously he had always been fastidious as to dress and cleanliness. The more advanced cases demonstrate defective judgment which often leads to abnormal behavior, and sexual misdemeanors of assault on minors occasionally occurs.

As stated previously, headache and dizziness are probably the earliest physical symptoms. Tinnitus or head noises are frequently bothersome and, incidentally, present an enigma from the therapeutic viewpoint. Attacks of vertigo and fainting can be explained by a vascular disturbance of the vestibular mechanism.

Physical signs vary considerably, depending on the degree of vessel involvement and the presence or absence of apoplectic attacks. It is possible for the uncomplicated cases to demonstrate unsteady gait, dysarthria, tremor of the hands, and less frequently tremor of the head. The pupils are small and sluggish in about 25 per cent of the cases. Sclerosis of the vessels of the optic fundi may or may not be apparent. As a general rule, sclerosis of the retinal vessels serves as a fair index of the condition of the cerebral arteries. The systemic blood vessels need not necessarily show sclerotic changes.

Those affected with cerebral arteriosclerosis are subject to convulsive disorders and apoplectiform attacks. Convulsions may be the most prominent feature of the disease. When such a symptom heralds disability, extreme care must be given to exclude other possible sources of convulsions, for example syphilis, brain tumor, cerebral atrophy, trauma, and alcoholism. Those persons having vascular accidents, whether they be the result of hemorrhage, thrombosis, or angiospasm, present a variety of symptoms and signs. Hemiplegia, hemiparesis,

apraxias, and aphasias are not uncommon, while muscular rigidity and contracture may be seen in advanced cases.

The majority of neurologic disturbances in arteriosclerotic persons result from thromboses with subsequent softening of brain tissue rather than from hemorrhage. Mild degrees of thrombosis or angiospasm probably account for the transitory neurophysiologic disturbances. Cerebrospinal fluid analysis may show a slight increase in the protein and cellular contents.

Here, as well as in the arteriolarsclerotic involvement of cerebral vessels, the clinical course is one of gradual deterioration and, broadly speaking, the prognosis is uniformly poor. Complicating renal or cardiac disease as well as intercurrent infections may shorten the course or cause death at any time.

Until the etiology of arteriosclerosis is more clearly understood, prophylaxis is limited to improving the mental and physical health of the patient in general. The treatment of cerebral arteriosclerosis holds no great promise to the one so afflicted. Improvement of the general physical and mental health and avoidance of physical exertion and emotional strain are of prime importance. Hobbies, occupational therapy, and mild exercise such as walking can be used to advantage.

Dietary regulation is essential. Should the patient have an exaggerated appetite, the food intake must be limited, particularly if there are complications such as cardiac or renal disease and hypertension. On the other hand, if the nutritional status is deficient, appropriate corrective steps should be taken. Supplementary vitamins in adequate amounts can be employed to good advantage in practically all cases.

Supervision even in the mild disorders of cerebral arteriosclerosis is wise and absolutely essential in those having moderate to pronounced mental and physical signs and symptoms. Careful consideration should be given to the selection of nurses and attendants who are to care for these patients. These assistants should have the attributes of understanding, a kind and cheerful manner, tolerance, willingness to accept some abuse with grace, and an immeasurable amount of patience and tact. The services of a nurse or attendant not only fulfill the requirements of supervision but also afford the patient a companion. This is extremely valuable in allaying fears and anxiety that may arise if the patient is left alone.

If the home facilities are suitable and adequate assistance is available, many of the psychoses and neurologic disorders of cerebral arteriosclerosis can be treated in the home. However, when the mental reactions and physical status reach the stage where it is difficult to manage the patient at home, hospital care should be recommended. Too much

emphasis cannot be placed on constant supervision of the patient with mental "disorganization" due to arteriosclerosis. Frequently he is destructive and in unguarded moments may wander away from home and commit acts that are dangerous to the general public or cause embarrassment for the relatives. Complications such as depression or severe paranoid trends most often necessitate hospital care. When the physical condition is not too poor, electroshock therapy may be successfully employed in combating depression.

The appointment of a legal guardian obviates many difficulties that arise in the handling of the patient's financial and business affairs. A guardian, if acceptable to the patient, also relieves him of worry and anxiety regarding business matters.

The physician must also bear in mind that he, too, must be patient and understanding. A few words of cheer, encouraging remarks, and a little time spent in talking to the patient accomplish much in easing the burden on the individual or his family. The physician's responsibility also entails an explanation of the cerebral arteriosclerotic process to the members of the family. By so doing, the burdens and verbal abuses that are often brought down on the patient when he does not do the proper thing may be avoided. The family should be made to understand that father or grandfather is not stubborn when he refuses to comply with requests made of him, nor is he deliberately being mean and nasty when he manifests irritability. They must realize that his foreign actions and behavior are a product of the illness and that kindness and patience on their part will accomplish far more than verbal abuse and threats.

Judicious use of certain pharmacologic preparations is often a valuable adjunct in the treatment of this condition. Barbiturates may be employed as sedatives and hypnotics. However, if these preparations are selected for use, it is inadvisable to administer them for more than several days at any one time. Continued use of barbiturates may lead to the development of toxic reactions, since the rate of excretion is low and the effect cumulative. Even though the taste be objectionable and the odor offensive, paraldehyde is probably the safest and most satisfactory hypnotic. Its acute toxicity is low, and since it is rapidly excreted the cumulative dangers are reduced to a minimum. If paraldehyde is given orally it is less objectionable when mixed with chipped ice in small amounts of milk or tea. It can also be given by rectum if mixed with a small amount of mineral oil. Intramuscular and even intravenous administration is possible when smaller doses are prescribed.

Although the presence of cardiac toxicity is debatable, it is the general belief that use of chloral for arteriosclerotic subjects is unwise. Small amounts of bromides may prove beneficial as sedatives in this

condition, but here again continued use is contraindicated, due to the cumulative effect.

Convulsive disorders associated with cerebral arteriosclerosis can in most instances be adequately controlled with dilantin or a combination of dilantin and phenobarbital.

The therapeutic value of the long-employed iodides is certainly questionable. Actually there is little evidence to support the theory that iodides cause absorption of inflammatory tissue.

Due to the cerebral vessel changes, namely the presence of sclerotic patches and loss of elasticity of the vessel wall, the blood flow to the brain is decreased. Compensation for this is often provided by increased blood pressure. Consequently, unless distressing symptoms appear it is unwise to attempt to reduce the blood pressure. In cases where the pressure is low the number of cerebral insults may be increased.

Normal physiology of circulation entails a drop of blood pressure while the subject is resting or sleeping. Consequently, more vascular accidents occur at this time, possibly as the result of reduced cerebral flow. This accounts also for episodes of nocturnal confusion demonstrated by many arteriosclerotic patients. The confusion may well be due to cerebral anoxia.

Caffeine, and particularly nicotinic acid, are capable of aiding in the production of increased blood flow. While the results with these preparations are not startling, a number of patients have been aided by their use. Caffeine can be easily supplied by giving the patient a cup of strong coffee. Investigation has shown that nicotinic acid is probably more effective than caffeine as a vasodilator. Paresthesias and blushing of the skin caused by nicotinic acid are at times sufficiently troublesome to the patient to prevent the use of this preparation. Hour-of-sleep doses of caffeine or niacin may be combined with a hypnotic, the latter being given to counteract the stimulant effects of these substances.

The introduction of the sulfonamides and penicillin as well as other advances in medical and surgical treatment have definitely increased life expectancy.

Within the past few years welfare authorities have been faced with a problem of steadily increasing importance, the care of psychotic old people. Statistical surveys have shown that the increase in hospital admissions of patients 65 years of age or older has exceeded the increase in all other types of admissions. Johnson[5] predicted that within less than a decade senile psychoses and psychoses with cerebral arteriosclerosis will relegate schizophrenia to second place in the number of new admissions to mental hospitals. In fact, he considers it likely that this problem will

place a greater burden on public mental hospitals than will returned veterans or any other single factor.

The establishment of geriatric units in all mental hospitals has been advocated by Johnson and others.[5] It is hoped that such innovations will produce new methods of treatment as well as lend more dignity and respect to the task of treating the senile. We, as practicing physicians, must of necessity adequately prepare ourselves to render satisfactory service in caring for the aged.

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OCULAR HEMORRHAGES

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Ocular hemorrhages are important not only because they produce visual loss but also because they usually indicate a disorder elsewhere in the body. One can roughly classify them in five main groups: external, vitreous, preretinal, retinal, and choroidal.

Of the external hemorrhages the most common is the subconjunctival hemorrhage, which is usually of no importance and may result from trauma or occur spontaneously. However, it is of great concern to the average patient. In older people subconjunctival hemorrhage suggests vessel weakness and warrants further investigation. A complete examination should be made for evidence of arteriosclerosis of the fundus as well as elsewhere in the body. Large hemorrhages may be caused by blows or falls on the head; these hemorrhages may also result from basal skull fractures with accompanying extravasation of blood along the floor of the orbit. Severe compression of the chest, scurvy, or purpura may also produce extensive hemorrhages. However, this never interferes with sight, and treatment consists of conservative measures such as warm compresses, dionin 2 per cent, or merthiolate ointment (ophthalmic 1:5000). Absorption of the extravasation usually requires about two weeks.

Vitreous hemorrhages of significant size interfere with the vision but are usually painless. They may result from trauma, arteriosclerosis, or inflammation of the retina, or may occur without apparent cause. In massive hemorrhages the light reflex is absent.

There is a severe type of recurring hemorrhage into the vitreous which occurs in adolescence, usually in males, and is known as Eales' disease. The disease tends to last many years and is often thought to be of tuberculous origin, e.g. tuberculous periphlebitis. The bleeding is most often from the ciliary body or occasionally from the retina. One should suspect an endocrine disorder, especially of the thyroid and pituitary glands, in this type of hemorrhage. Hemorrhages into the vitreous from the retina are usually of the preretinal or subhyaloid type, that is, occurring between the retina and the vitreous. The bleeding is usually of venous origin and represents long-standing vascular disease. The shape of the clot is ordinarily that of a half circle with the straight portion above. Vitreous hemorrhages occur in the macular region and are usually of considerable size and, because of their location, interfere seriously with vision. They usually are absorbed but tend to recur and

may break through into the vitreous. This type may be due to trauma but is most frequently due to arteriosclerosis and is not uncommon in cases of subarachnoid hemorrhage. Rest is an important factor in treatment.

One of the serious sequelae of vitreous hemorrhage is retinitis proliferans, in which there is a connective tissue proliferation which may lead to retinal detachment. The unabsorbed blood is organized by the growth of fibroblasts into it and the formation of new blood vessels. In diabetes complicated by retinitis proliferans the blood vessels are formed first, followed by the connective tissue.

Occlusion of a Vessel

The two main vessels of special concern are the central retinal artery and vein, either of which may be occluded and cause hemorrhages in the eye. Occlusion of the artery is serious. There is a sudden loss of sight. Upon examination the arteries appear narrowed, with smaller ones obliterated, and usually all arteries appear darker than normal. The disk is pale, and the retina is milk-white. The macula is prominent, and the "cherry-red spot" is present due to a red reflex from the choroid. It may also occur in amaurotic family idiocy. There may or may not be hemorrhages, which, if present, are usually small and near the disk. Pressure on the eyeball will empty the veins if the occlusion is incomplete. This occlusion of the retinal artery may occur with mitral stenosis.

Occlusion of the central vein may be complete or involve only one of its branches, and onset with loss of vision is usually less abrupt than that of occlusion of the artery. Examination reveals a typical picture of swollen disk and enormously dilated, tortuous veins of a dark red color. The retina is literally covered with superficial and deep hemorrhages of all sizes and shapes which often occur also on the disk. The superficial hemorrhages are striate and flame shaped, whereas the deep hemorrhages are round and irregular. The arteries are narrow. Sight is impaired, usually unilaterally but sometimes bilaterally. If pressure is placed on the globe the veins will not collapse. In some cases only a branch may be involved, in which event there is little disturbance of vision. With macular involvement after absorption there is likely to be a "hole" in the macula having a red, punched-out appearance and due to degeneration following edema. Many of these cases are complicated by secondary glaucoma, offering a serious prognosis. Today many of these eyes are saved by the use of heparin, dicumarol, and deep diathermy.

Hemorrhages in the Uveal Tract

Hemorrhages in the uveal tract may be due to (1) overdistention of vessels, e.g. in iris, (2) fragility of vessels, e.g. arteriosclerosis, or (3) in-

volvement of the blood itself, producing changes in the blood vessel walls, e.g. anemia, leukemia, purpura. Such hemorrhages may be traumatic or spontaneous and may occur in the iris and produce hyphemia. They usually are absorbed but may persist and produce blood-staining of the cornea.

Choroidal hemorrhages are important clinically because, if of significant size, they may produce permanent visual defects due to destruction of the overlying retina. Choroidal hemorrhages are dark red in color, rounded, and invariably occur beneath the retinal vessels. These hemorrhages deprive the overlying retinal tissue of nourishment by pressure. Retinal hemorrhages are usually striated or flame shaped, and the superficial vessels rarely cross over them. Choroidal hemorrhages may be differentiated from tumor by their sudden onset and the fact that under transillumination they are usually more translucent than tumors. Absorption may take several months. They usually leave a scar which is smaller than the original hemorrhage, as shown by the following case, but if the macula is involved the damage to sight may be a great handicap.

Case Report

A man, aged 34, was first seen on November 12, 1946, complaining of a "blind spot" in the left eye. Examination at this time revealed a peripapillary hemorrhage on the temporal side. Visual acuity at this time was O.D. 6/6, O.S. 6/6.

On November 27, 1946 the patient returned with marked reduction in visual acuity of the left eye, the vision being reduced to 6/12. Fundus examination revealed an extensive choroidal hemorrhage starting just temporal to the disk and extending over to involve the macula. Visual field studies revealed a centrocecal scotoma (fig. 1). The patient was

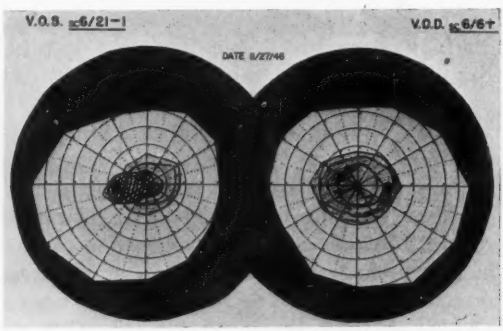

FIG. 1. O. S. Absolute centrocecal scotoma
Test objects: form 1/280
color 3/280
C.P. 10 ft.
Cooperation good
Features normal

given a course of intravenous typhoid therapy and deep diathermy to the eye. Progressive improvement was noted and a subsequent visual field study on March 31, 1947, showed only a paracentral scotoma and visual acuity restored to 6/6-1 (fig. 2).

Choroidal hemorrhages may be associated with acute choroiditis, vascular sclerosis, myopia, papilledema (rare), and the blood dyscrasias. A choroidal hemorrhage may be massive, but this usually occurs after operation.

Retinal Hemorrhage

Retinal hemorrhages of pathologic significance arise from the capillaries and are usually due to a dysfunction of the capillaries themselves rather than to arterial hypertension.

Duke-Elder[1] lists seven classes of conditions associated with capillary hemorrhages: (1) trauma, (2) obstruction, as thrombosis, papilledema, subarachnoid hemorrhage, (3) inflammatory conditions in the retina, (4) toxic states, e.g. acute febrile conditions such as malaria, influenza, (5) vascular retinopathies, e.g. nephritis, diabetes, arteriosclerosis, hypertension, (6) senile arteriosclerosis, and (7) blood dyscrasias.

The appearance of retinal hemorrhages varies according to their site. They are usually central and if they involve the superficial layers are striate and flame shaped, whereas in the deeper layers they are round and irregular. In contrast to the dark choroidal hemorrhages they are of a bright red color. They may last for months but have been known to disappear in three to four days.

The vascular retinopathies are characterized by hemorrhage and exudate in addition to sclerosis, hypertension, and toxemia.

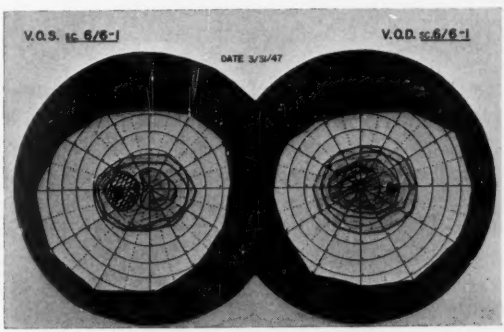

FIG. 2. Test objects: form 1/280
color 3/280
C.P. 10 ft.
Cooperation good
Features normal

The main changes in diabetic retinopathy are hemorrhages and exudates.[2] The condition is usually bilateral, and the hemorrhages are often punctate, tending to occur first in the periphery, especially between the temporal vessels and about the disk. They may be of any size, mostly round, small, and deep, and may be superficial and flame shaped, as the retinitis of nephritis. The hemorrhages are usually behind the retinal vessels, and there is usually little if any retinal edema. However, edema and exudates may be present, but they differ from those of renal retinopathy in being clear-cut patches rather than the cotton-wool type. A prominent feature associated with diabetes is early engorgement of the veins. There is no visual disturbance unless the macula is involved, and there is no constant relationship between the duration and severity of the diabetes. Hemorrhages may occur even when the condition is controlled. They are often situated away from the larger vessels and represent an escape of blood by diapedesis. Extensive hemorrhages may occur in the presence of arteriosclerosis.

Hypertension

Benign and essential hypertension are distinguished by the presence or absence of papilledema. Hemorrhages are usually superficial and flame shaped in the nerve fiber layer. There are many cotton-wool spots, and there may be deep hemorrhages and a star-shaped figure in the macula.

Blood Dyscrasias

In pernicious anemia the disk is pale and the fundus yellow. Retinal vessels show little change; veins may be engorged or tortuous. Hemorrhages are not numerous, have a regular distribution, tend to occur in the posterior pole, and are usually small and superficial. They seldom affect vision.

In leukemia the veins are dilated and tortuous, bright red, and often constricted at intervals. The arteries are small and pale. Hemorrhages are radial, small, linear, round, and irregular. They have a characteristic white center due to accumulated leukocytes, which may also occur in pernicious anemia.

In polycythemia vera, hemorrhages are rare. The fundus has a purplish color and the veins are dilated.

Treatment of hemorrhages due to blood dyscrasias depends upon the determination and subsequent correction of the causative factor.

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MANAGEMENT OF PATIENTS WITH PROSTATIC OBSTRUCTION

Review of 395 Cases

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In 1945 I reviewed a series of 214 patients with prostatic hypertrophy upon whom I had operated from January, 1943, to January, 1944.[1] The following series of 395 patients were operated upon from January, 1944, to December, 1945. This review will compare these series, especially from the standpoint of coexisting diseases, the type of surgical procedure employed, the end results, and the mortality.

In recent years marked progress has been observed in the management of patients with bladder neck obstruction. The introduction of new antibiotic agents, adequate preoperative and postoperative management, and refinements in surgical technic have been accompanied by a progressive lowering of the operative mortality and morbidity in patients suffering from urinary obstruction.

Usually the onset of obstruction is insidious. Many men of the older age group believe nocturia, diminution in the force of the urinary stream, and dribbling to be only an indication of advancing age and fail to seek medical advice until complete obstruction occurs. Occasionally a sudden attack of urinary retention may be precipitated by exposure to cold, overindulgence in alcoholic beverages, other surgical procedures requiring confinement to bed, or other factors irritating to the bladder mucosa.

Examination

A complete physical examination is essential to ascertain the general vitality of the patient. As will be observed in the following statistics, cardiovascular and renal complications comprise the major complicating diseases in these elderly men.

A careful rectal examination is also essential to determine the extent of any proposed surgical procedure. The size of the prostate may be misinterpreted upon rectal examination, as the median lobe and subcervical enlargements protruding into the bladder cannot be palpated. Benign hypertrophy of the prostate usually involves the median and lateral lobes, while carcinoma of the prostate more frequently arises in the posterior lobe.

The size of the prostate, as determined by rectal examination, according to Lowsley,[2] has nothing to do with its tendency to cause ob-

struction. As I reported previously,[1] the symptoms produced by prostatic hypertrophy are not proportional to the degree of enlargement. Thus a large gland that does not encroach on the bladder outlet produces less pronounced obstructive symptoms than those produced by a smaller gland that does encroach on the bladder outlet. Generally after rectal examination the patient voids, and a small catheter is introduced into the bladder to determine the amount of residual urine.

Catheterization, cystoscopy, or other instrumentation must be undertaken with caution in patients with prostatic obstruction. Not only may such measures precipitate an attack of acute retention, but they may provoke an exacerbation of a urinary tract infection with accompanying chills and fever. Cystoscopy is never an emergency procedure although invaluable in determining the type of hypertrophy, the condition of the bladder, and in imparting information as to indications for the proper surgical procedure.

In elderly men with long-standing obstructive symptoms I never recommend cystoscopic study prior to the investigation of renal function. Intravenous urography is utilized in all cases to elicit information concerning renal damage and function, to note whether dilatation of the ureters or hydronephrosis is present, and to detect the presence of vesical diverticula or calculi in the urinary tract. To neglect such studies may result in incipient uremia.

Diagnosis

Little difficulty is encountered in establishing an accurate diagnosis. A careful history and a careful urologic survey suffice to establish the diagnosis of prostatic obstruction.

Carcinoma of the prostate may occur simultaneously. This can usually be ruled out by rectal examination, x-ray studies for metastasis, and acid and alkaline phosphatase determinations. Prostatic abscess and calculi are usually recognized by rectal palpation and roentgenographic investigation. Chronic prostatitis may be diagnosed by examination of the expressed secretion. A stricture of the urethra is diagnosed by the passage of a catheter. Syphilis may produce the characteristic condition of the bladder found in cord lesions with accompanying residual urine. These symptoms respond well to transurethral resection of the bladder neck. The Wassermann test, spinal fluid studies, and cystometric investigations establish the diagnosis.

Treatment

Many patients with enlargement of the prostate, with negligible obstructive symptoms, and with little or no residual urine do not require surgical intervention. Conservative treatment such as sitz baths, gentle

prostatic massage, and hormonal therapy should be recommended. Prophylactic transurethral resection in such cases is unwarranted and should be condemned.

Preoperative management is influenced by the general condition of the patient, renal function, and urinary tract infection.

If blood studies reveal nitrogen retention, intermittent or continuous catheter drainage is advocated. In instances in which prolonged urethral catheter drainage seems necessary I prefer suprapubic puncture. This is attended by no operative risk and may be performed under local anesthesia. The patient is more comfortable, and urethritis and the incidence of epididymitis is minimized.

Three procedures are available for the surgical relief of prostatic obstruction: transurethral resection of the prostate, suprapubic prostatectomy, and perineal prostatectomy. No single operative procedure is suitable for all cases of prostatic hypertropy. I believe further that 85 to 90 per cent of patients with prostatic obstruction may be completely relieved by transurethral resection, which is in reality a transurethral prostatectomy, if recurrences are to be avoided. Suprapubic prostatectomy is recommended if the gland is extremely large, or lesions on the urethra, such as false passages or multiple strictures, prevent the introduction of the resectoscope.

Perineal prostatectomy is confined to early cases of carcinoma, when the disease is localized in the gland, metastases are absent, and it is technically possible to remove completely the entire gland and seminal vesicles.

Anesthesia

In the majority of cases spinal anesthesia was employed. In some instances pentothal or a combination of pentothal and curare was employed when the medical consultant advised against the use of spinal anesthesia. The same anesthesia may be recommended for the transurethral removal of median lobes, resection of a contracted bladder neck, and excision of a small fibrous prostate.

When the patient leaves the hospital the obstructive symptoms should be completely relieved and control of urination normal. If present, pyuria may be eradicated during the postoperative period or treatment continued under the supervision of the family physician. Postoperative observation is essential, and I require the patient to return in one month for routine observation.

At Cleveland Clinic from January, 1944, to December, 1945, I operated upon 395 patients with benign prostatic hypertrophy. An analysis of the findings follow.

Age

The average age was 65.9 years. The oldest patient was 84 and the youngest 34 years of age. The latter patient had a contracted bladder neck and 310 cc. of residual urine.

General Complications

Involvement of cardiovascular system

1. Generalized arteriosclerosis 36
2. Hypertensive arteriosclerotic heart disease 58
3. Hypertensive arteriosclerotic heart disease with angina pectoris and heart block 1
4. Hypertensive arteriosclerotic heart disease with valvular disease 4
5. Hypertensive arteriosclerotic heart disease with coronary disease 8
6. Hypertensive arteriosclerotic heart disease with auricular fibrillation 4
7. Hypertensive arteriosclerotic heart disease with auricular fibrillation and coronary disease 2
8. Hypertensive arteriosclerotic heart disease with congestive failure 1
9. Arteriosclerotic heart disease 30; valvular lesions 2
10. Arteriosclerotic heart disease with coronary disease 4
11. Arteriosclerotic heart disease with congestive failure 1
12. Arteriosclerotic heart disease with heart block 1
13. Arteriosclerotic heart disease with angina pectoris 1
14. Coronary disease 3
15. Hypertensive heart disease 2
16. Essential hypertension 6
17. Hypertensive heart disease with congestive failure 1
18. Rheumatic heart disease 2
19. Arteriosclerotic hypertension 59

Total 226

Other Complications

1. Diabetes mellitus 18
2. Osteoarthritis 32
3. Hypertrophic arthritis 24
4. Vesical calculi 25
5. Hernia-inguinal, unilateral 40

6. Hernia-inguinal, bilateral 19
7. Secondary anemia 9
8. Hydronephrosis, unilateral 9
9. Hydronephrosis, bilateral 8
10. Urethral stricture 10
11. Emphysema 3
12. Parkinson's disease 3
13. Duodenal ulcer 2
14. Gastric ulcer 2
15. Pyelonephritis 4
16. Pernicious anemia 2
17. Vesical diverticulum 16
18. Hemorrhoids 13
19. Vesical papillomata 3
20. Carcinoma of bladder 4
21. Carcinoma of cecum 1
22. Carcinoma of rectum 3
23. Previous nephrectomy 2
24. Nonfunctioning kidney 3
25. Renal calculus 3
26. Ureteral calculus 2
27. Prostatic calculi 2
28. Chronic epididymitis 4
29. Thrombophlebitis 9

In this series, as in those reported in 1945, heart disease and hypertension were the major complicating factors. For this reason every patient was examined by the cardiologist prior to operation.

Seventy-two patients in this series of 395 had complete urinary retention. The residual urine averaged 273 cc., the largest residue being 1350 cc.

I prefer to avoid sudden decompression when the bladder has been overdistended for a long period of time. Rather than resorting to prolonged urethral catheter drainage, a suprapubic puncture was performed on 36 patients. An indwelling catheter was used in 274 patients and intermittent catheter drainage in 8. Suprapubic cystotomy was performed in 12, suprapubic cystolithotomy and first stage prostatectomy in 7.

Operations performed:

1. Suprapubic prostatectomy
   a. One-stage operation 44
   b. Two-stage operation 15

2. Suprapubic prostatectomy and cystolithotomy 6
3. Suprapubic prostatectomy following transurethral resection 2
4. First stage prostatectomy 3
5. Transurethral resection
   a. One-stage operation 263
   b. Transurethral resection and litholapaxy 10
   c. Transurethral resection and fulguration of bladder tumor 4

Total 395

In this series the surgical procedure instituted was approximately the same as the operative procedures employed in the previous series of 214 cases.

1. Suprapubic prostatectomy
   a. One-stage operation 10
   b. Two-stage operation 6
2. Perineal prostatectomy 1
3. Transurethral resection
   a. One-stage operation 183
   b. Two-stage operation 14

Total ..... 214 cases

The amount of tissue resected is governed by the size and type of the prostatic hypertrophy. As a general rule, for contracted bladder neck, median lobe hypertrophy, and transurethral resection for bladder conditions associated with syphilis and the cord lesions accompanied by incomplete emptying of the bladder, smaller amounts of tissue are removed. An average of 22.9 Gm. was removed by transurethral resections, and the largest amount removed was 98 Gm. An average of 64.1 Gm. was removed by suprapubic prostatectomy. The largest gland weighed 197 Gm. Sixteen patients had had a transurethral resection performed previously. I had operated on 2 eight years ago, and 14 had had a transurethral resection performed elsewhere.

Postoperative bleeding occurred in 22 cases. In 1 patient bleeding occurred on the day of operation but stopped upon introducing the resectoscope and fulgurating the bleeding points. In 21 patients some bleeding occurred from the second to the twenty-sixth day and was easily controlled by the introduction of an indwelling catheter. A blood transfusion was administered before, during, or after operation in 63 cases.

The postoperative complications were:

1. Bronchopneumonia	1
2. Pulmonary embolus	2
3. Extravasation of urine	1
4. Pyelonephritis exacerbation	12
5. Thrombophlebitis	6
6. Cardiac arrhythmia	2
7. Congestive failure	1
8. Pleurisy	1
9. Acute urinary tract infection (exacerbation)	18
10. Shock	1
11. Toxic hepatitis	1

Mortality and Morbidity

Nine patients died following operation, a mortality of 2.02 per cent. The remainder were discharged from the hospital in satisfactory condition.

Cause of Death

1. Coronary occlusion	2
2. Septicemia, Endocarditis, Pneumonia	1
3. Pulmonary atelectasis	1
Terminal pneumonia	1
Uremia	2
Cerebral accident	1
Pulmonary embolus	1

Temporary incontinence occurred in 2 cases but cleared up within three weeks.

Conclusions

1. Medical consultation is essential to maintain a low operative mortality and should be directed chiefly toward the cardiovascular system.

2. Eighty-five to 90 per cent of patients with prostatic obstruction may be completely relieved of symptoms by transurethral resection.

3. In a series of 214 patients operated upon from January, 1943, to January, 1944, for prostatic obstruction the operative mortality was 2.52 per cent. In a similar series from January, 1945, to December, 1946, of 395 cases the mortality was 2.02 per cent, a combined mortality for 609 cases of 2.28 per cent.

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A CLASSIFICATION OF DISEASES OR CONDITIONS CHARACTERIZED BY HEMORRHAGE

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The hemorrhagic studies which are of greatest value in the diagnosis of diseases characterized by abnormal bleeding are skin bleeding time, test tube coagulation time, measurement of the amount of serum expressed from the clot, platelet count, capillary fragility test, and the estimation of prothrombin concentration. Tests of occasional value are the coagulation time of recalcified oxalated plasma after rapid and slow centrifugation, the estimation of fibrinogen concentration, and the demonstration of the presence of anticoagulant substances. The methods used in the hematology laboratory of Cleveland Clinic and the range of normal values for these laboratory procedures are given in table 1.

A classification of hemorrhagic diseases based upon the principal coagulation and hemostatic components involved, as revealed by standard laboratory tests, is given in table 2. The grouping of diseases with hemorrhagic manifestations on the basis of pathologic physiology is a modification of classifications by Quick,[1] Lucia and Aggeler,[2] Wintrobe,[3] and others.

Local vascular abnormality is suggested when the patient is bleeding from a single focus and no abnormalities are revealed when hemorrhagic studies are made. Generalized vascular abnormality is suggested when there are multiple purpuric manifestations, a prolonged skin bleeding time, and a positive capillary fragility test. If the platelets are normal the purpura is of the nonthrombopenic type. If the number of platelets is decreased, the purpura is of the thrombopenic type. Platelet deficiency is revealed by a low platelet count, defective clot retraction, and a wet and flabby clot. A prolonged coagulation time is indicative of abnormalities in the circulating blood of such factors as fibrinogen, prothrombin, and anticoagulants.

The coagulation time of recalcified oxalated plasma after rapid and slow centrifugation is of use in the diagnosis and differential diagnosis of hemophilia. In hemophilia the platelets do not disintegrate and liberate their thromboplastin as readily as they do in normal blood. On centrifugation at rapid speed the more resistant platelets are separated more effectively than in nonhemophilic conditions; the coagulation time of recalcified plasma of hemophilic blood which is rapidly centrifuged is therefore appreciably greater than recalcified plasma which is slowly centrifuged.

Table 1
TESTS ROUTINELY USED IN HEMORRHAGIC STUDY

Test	Method	Normal Value
Skin bleeding time	Ivy	2-6 minutes
Coagulation time	4 tube method using venous blood	5-15 minutes
Clot retraction	3-5 cc. venous blood in graduated tube	40-60 ml. serum/100 ml. expressed from clot in 4 hours, room temperature
Platelet count	Reese-Ecker	200,000 to 400,000 per cu.mm.
Capillary fragility	Blood pressure cuff above elbow; 40 mm. Hg for 5 minutes. If no petechiae, 100 mm. for 5 minutes.	No petechiae
Prothrombin concentration	Quick	80-120 per cent
TESTS OF OCCASIONAL VALUE		
Coagulation time of recalcified oxalated plasma	Quick	2-4 minutes. Less than 15 seconds difference between rapid and slow centrifugation
Fibrinogen concentration	Cullen and Van Slyke	0.3-0.5 Gm./100 ml.
Test for anticoagulants	Coagulation time of recalcified normal plasma to which plasma of patient is added	No increase in clotting time of normal plasma

Table 2

CLASSIFICATION OF DISEASES OR CONDITIONS CHARACTERIZED BY HEMORRHAGE

Principal Factor	Laboratory Findings	Diseases or Conditions
I. VASCULAR ABNORMALITY		
A. Local	Hemorrhagic studies reveal no abnormality	Trauma Ulceration, necrosis Thrombosis, embolism (embolic purpura) Defects in vascular wall Increased intravascular pressure Tumors Hereditary hemorrhagic telangiectasia Certain skin diseases Purpura annularis telangiectoides Progressive pigmentary dermatosis Hyperelasticity of the skin Functional uterine bleeding
B. General		
1. Without decrease in platelets (Nonthrombopenic vascular purpuras)	Tourniquet test usually positive Bleeding time variable Clotting time and other tests usually negative	Nonthrombopenic purpuras secondary to: Infections Chemicals Toxemias Nephritis Cushing's syndrome Allergic (anaphylactoid) purpuras Vitamin C deficiency (scurvy) Purpura simplex (easy bruisability)

	Bleeding time prolonged Tourniquet test variable Other tests usually negative	Hereditary purpura with prolonged bleeding time (pseudohemophilia)
2. With decrease in platelets (Thrombopenic purpuras)	Platelets decreased Bleeding time prolonged Tourniquet test usually positive Defective clot retraction Clotting time normal or only slightly prolonged Other tests usually negative	Thrombopenic purpuras secondary to: Infections Chemicals (sedormid, quinine, sulfa drugs, organic arsenicals, gold salts, colchicine, salicylates, etc.) Sensitivity to foods or inhalants Physical agents Artificially induced fever Radioactive substances Diseases characterized by hypoplasia of bone marrow Diseases characterized by splenomegaly Neoplasia Leukemias Carcinoma Myeloma, etc. Miscellaneous diseases Cirrhosis of liver Nephritis Hodgkin's disease Lupus erythematosus Idiopathic hemorrhagic purpura (Essential thrombopenic purpura) Congenital thrombopenic purpura
II. PROTHROMBIN DEFICIENCY	Plasma prothrombin decreased (prolonged prothrombin time)	Vitamin K deficiency Obstructive jaundice

(*Continued on Page 192*)

Table 2—(Continued)

CLASSIFICATION OF DISEASES OR CONDITIONS CHARACTERIZED BY HEMORRHAGE

Principal Factor	Laboratory Findings	Diseases or Conditions
	Prolonged coagulation time of recalcified oxalated plasma If moderate prothrombin deficiency, no alteration in bleeding time, coagulation time, or other tests If severe prothrombin deficiency, may have prolonged bleeding time, prolonged clotting time, and defective clot	Biliary fistula Intestinal disease Sulfa drugs Hemorrhagic disease of the newborn Liver disease, severe Drugs Dicumarol Salicylates Congenital (essential) hypoprothrombinemia
III. FIBRINOGEN DEFICIENCY	Plasma fibrinogen reduced below 0.1 Gm. per 100 ml. Coagulation time prolonged Clot defective Bleeding time variable	Liver disease, severe Diseases involving bone marrow Congenital fibrinogenopenia
IV. THROMBOPLASTIN DEFICIENCY		Hemophilia ? (See VII)
V. CALCIUM DEFICIENCY		(No well defined hemorrhagic disease)
VI. EXCESS ANTICOAGULANTS	Coagulation time prolonged Increased coagulation time of recalcified normal plasma to which plasma of patient is added Other tests usually negative	Hemorrhage, unknown cause with demonstrable excess anticoagulant Excess heparin Heparin therapy Anaphylactic shock
VII. UNCLASSIFIED	Coagulation time prolonged Coagulation time of recalcified oxalated plasma prolonged. Longer after rapid than after slow centrifugation Bleeding time and other tests usually normal	Hemophilia Hemophilia-like syndrome in female

Schönlein's purpura, Henoch's purpura, Osler's erythemas, Frank's capillary toxicosis, David's disease, and Glanzmann's hereditary thrombasthenia are not included in the classification, for the clinical syndromes described by these authors are ill defined in terms of etiology, pathology, or laboratory findings by modern methods. Terms such as "purpura fulminans", "purpura senilis", "orthostatic purpura", and "mechanical purpura" are likewise not considered, for these terms are obviously descriptive and nonspecific.

In practice it is not always possible to fit all diseases characterized by hemorrhage snugly into one or the other pigeonholes of classifications, for there are combinations and varying degrees of abnormality of coagulation components, and there may be more than one etiologic agent. Also, the laboratory tests are subject to variations depending upon the exact technic used and the manner of interpreting results.

In making the final diagnosis, the family and personal history, the physical examination, and other laboratory and radiologic studies are to be evaluated along with tests for hemorrhagic abnormality. The response to therapy, the course of the disease, and the changes that occur when possible etiologic agents are eliminated are also of value. No diagnosis of primary or hereditary hemorrhagic disease should be made until all other possibilities have been excluded, for hemorrhage is usually secondary to and a manifestation of disease entities, the etiology of which can be demonstrated.

Summary

A classification of disease or conditions characterized by hemorrhage based upon laboratory tests and essential coagulation and hemostatic components involved is presented.

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ELECTROENCEPHALOGRAPHY

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Electroencephalography, or the recording of action potentials of the brain, is being utilized increasingly as a laboratory aid in studying a variety of cerebral dysfunctions.

Hans Berger[1] first reported in 1929 that he had recorded spontaneous electric discharges from the human brain and established that this electric activity originates in the neurons.

Satisfactory amplification of the extremely small potential changes depends upon a very sensitive and delicate instrument capable of responding to minute potential changes. The instrument consists of a preamplifier, an amplifier, and a recording pen. The most satisfactory instruments consist of several channels and are able to record voltage changes simultaneously from several points. The instrument can record frequencies of 1 to 40 per second and will respond to changes in potential from 5 to 300 microvolts. Each record is carefully standardized before and after the recording so that voltage of the waves can be determined, and the recording paper runs at a constant speed so that the frequency of the waves can be counted.

The usual record takes only thirty to sixty minutes to record and is taken without pain or discomfort to the patient. The patient is usually placed in a shielded room to exclude extraneous electrical impulses which might produce artifacts in the record. The record is made with

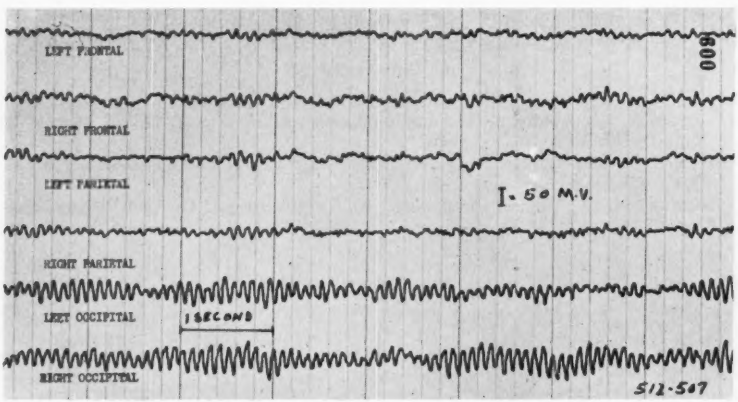

FIG. 1. Normal 10 per second alpha waves best seen in the occipital leads.

the patient relaxed but not asleep, as free from all sensory stimuli as possible, and within two hours after a meal. The patient should be free from the effect of medication before the record is made. Small electrodes are attached to the frontal, temporal, parietal, and occipital regions of both sides of the scalp in a routine examination. An indifferent electrode is attached to the lobe of the ear and is used as a point of reference. The patient is grounded by an electrode attached to the other lobe of the ear. Additional electrodes are used for cortical localization.

The normal pattern of the electroencephalogram consists of a series of sinusoidal waves with a frequency of 8 to 12 per second (average 10) and with an amplitude of 10 to 75 microvolts (fig. 1). These waves are most regular from the occipital and parietal regions with the patient's eyes closed. These are called alpha or Berger waves. About 85 to 90 per cent of the population in general show normal patterns; the other 10 to 15 per cent show irregularities in the electroencephalographic pattern.[2] The records are analyzed as to frequency, amplitude, wave forms, and in some cases the phase relationship of abnormal waves.

Convulsive disorders or the epilepsies show the most striking changes. Even in the interval between seizures the electroencephalogram will show a high percentage of abnormalities (80 to 85 per cent). Most cases show variations in frequencies, called dysrhythmias. The waves are either too fast or too slow. Gibbs[2] correlated the abnormal epileptic patterns and found that rapid spike waves were more often associated with grand mal seizures, a slow (four to six-second) wave (fig. 2) was found in psychomotor seizures, and a slow (three-second) wave (fig. 3), often with an alternating diphasic spike, was associated with petit mal activity. However, prediction of the clinical type from the record between seizures is not always possible. The voltage is usually abnormally

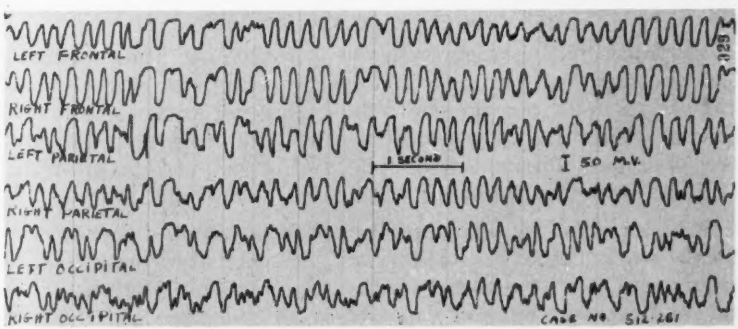

FIG. 2. Case of 16-year-old patient with grand mal, petit mal, and psychomotor seizures; the latter were dominant recently.

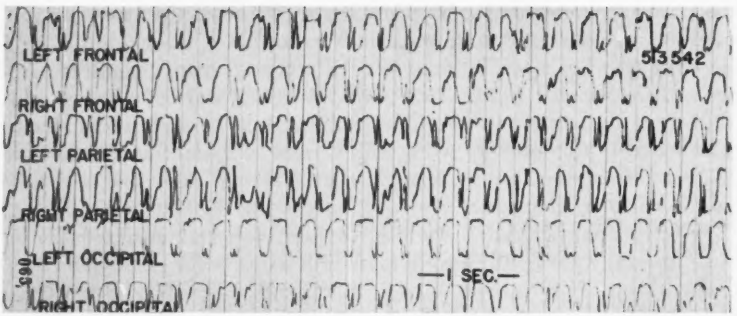

FIG. 3. Record of a clinical petit mal seizure which occurred during hyperventilation.

high in epileptic records, sometimes reaching 200 to 300 microvolts. During an actual seizure there is a tremendous energy output, indicating a massive neuronal discharge. Hyperventilation will often produce a disorganization of the normal pattern and an abnormal voltage build-up which otherwise might not appear. Clinical or subclinical seizure discharges are often produced in petit mal epilepsy by over breathing.

Focal organic lesions, such as tumors, abscesses, and cysts, when they involve the cortex, can often be localized by the focal abnormal electric activity produced by the lesion.[3] The lesion, itself, may be electrically inactive, but the surrounding compressed brain tissue usually gives rise to abnormal, slow waves. Amplitude asymmetry between homologous areas of the two hemispheres is also useful in cortical localization. An epileptogenic lesion may occasionally give rise to focal discharges of spike-like waves. A subdural hematoma may cause a depression of electrical activity over the area of the injury.

Electroencephalography is an aid in evaluating head trauma. As might be expected, posttraumatic epilepsy and cases with neurologic evidence of brain damage show the higher percentage of abnormal records. Walker[4] has used a subconclusive dose of metrazol to activate areas of abnormal irritability or epileptogenic foci, and this localization is utilized in the neurosurgical removal of these lesions.

A high percentage of abnormal records have been demonstrated in cases of psychopathic personalities and behavior disorders in children. Putnam and Merritt[5] reported a series of cases in which dullness, apathy, and mild mental confusion appeared as an epileptic variant. Electroencephalography furnishes valuable diagnostic information in many of these epileptoid conditions.

Conclusion

Electroencephalography is a valuable laboratory diagnostic instrument in the study of convulsive disorders, in the localization of gross lesions of the cortex, in the evaluation of head injuries, and in the diagnosis of other conditions which indicate a cerebral dysfunction. It is not intended that electroencephalography should displace other means of investigation such as a careful history, neurologic examination, x-ray examination, blood and spinal fluid studies, but rather that it should serve as a supplementary procedure to the proved methods of diagnosis in diseases of the nervous system.

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PLASMOCYTOMA OF THE CLAVICLE

Report of a Case

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Solitary plasma cell myeloma of the bone is a rare disease, approximately 50 cases so designated having been recorded in the literature. Only 1 instance of myeloma beginning as an apparently solitary lesion in the clavicle is on record[1] so far as can be determined. In the case to be presented the lesion appeared to be limited to the clavicle except for possible invasion of the sternoclavicular joint. Considering the difficulty of positively ruling out other osseous involvement, the term plasmocytoma, without further qualification, is considered a more accurate designation than solitary plasma cell myeloma.

The following case presents an interesting example of this type of primary neoplasm of the bone.

Case Report

A colored housewife, aged 46, entered Cleveland Clinic on August 2, 1946, to consult Dr. T. E. Jones because of pain and swelling of the right shoulder. Three years before entry she had first experienced pain in the right shoulder with radiation up the neck and behind the right ear, and at that time a diagnosis of arthritis had been made. There was transient swelling over the clavicle. After a year the pain became so severe that she had to limit her activities for two weeks. Following this rest, the pain and swelling subsided. During the two years before entry pain had recurred intermittently, and during the year before admission the swelling had gradually increased in size. Following hard work it enlarged temporarily. At the time of entry the patient stated that she had no pain unless she moved her shoulder or lay down without a pillow.

Except for occasional pain in the joints she had always been well. There had been no weight loss.

Physical examination revealed an obese colored woman, 5 feet 7 inches in height and weighing 248 pounds. Over the right clavicle was a large mass 12 x 9 x 6 cm., firm, fairly smooth, fixed to the medial aspect of the right clavicle and extending to the level of the third rib inferiorly, to the midline medially, and as high as the suprasternal notch. There was no apparent attachment to the thyroid gland. The skin was freely movable over the mass. On movement of the right shoulder the patient experienced slight pain in the region of the mass. Except for extreme obesity, the physical examination was negative. The temperature, pulse rate, and respirations were normal.

Roentgen Examination

The proximal two-thirds of the right clavicle showed extensive bone destruction with some new bone formation and an associated soft tissue mass. The new bone appeared as irregular strands infiltrating into the soft tissue mass. Other bones of the thorax were not involved.

X-ray examination of the chest was not entirely satisfactory. There was no evidence of pulmonary metastasis. The hilar lymph nodes did not appear enlarged. Progress studies were advised.

The roentgenologic diagnosis was malignant neoplasm of the right clavicle, possibly secondary degeneration of a benign tumor, appearance consistent with chondrosarcoma. The tumor mass was regarded as of probable primary origin in the clavicle rather than metastatic, though the latter possibility could not be excluded (fig. 1).

Sixteen days after the first Clinic visit the patient was admitted to the hospital for operation by Dr. T. E. Jones. At this time routine urinalysis was negative. Examination of the blood revealed a red cell count of 3,720,000 with 11 Gm. per cent hemoglobin and a white cell count of 4150. Blood Wassermann and Kahn tests were negative.

Findings at Operation

On the day following admission an operation was performed. An incision was made over the right clavicle from a point over the right shoulder to a point over the attachment of the sternomastoid muscle. The skin and subcutaneous tissues were reflected by sharp dissection, exposing a fusiform tumor of the right clavicle 16 x 8 x 8 cm. The lateral portion of the clavicle was exposed and divided approximately 5 cm. from the acromial

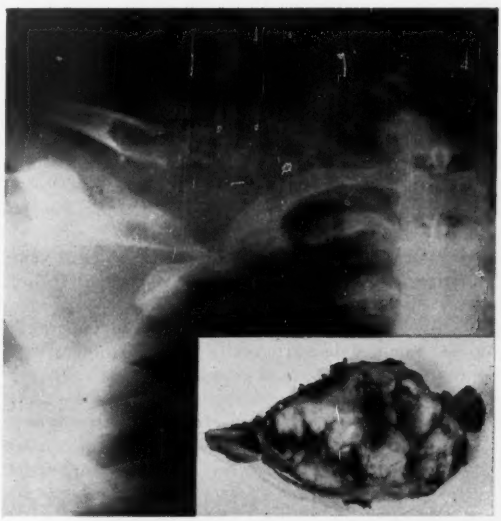

FIG. 1. Roentgenogram of right clavicular area.
Inset. Gross specimen showing replacement of greater portion of clavicle by tumor.

joint. The clavicle was then disarticulated from the sternum. At this point there appeared to be some invasion across the joint, therefore the joint cartilage was excised and a portion of the adjoining sternum curetted away. The area was thoroughly coagulated with the electric cautery. The remaining distal portion of the clavicle was removed by disarticulation at the acromioclavicular joint.

Pathologic Report

Gross examination. The major portion of the specimen was roughly ovoid, measured 12 x 6 x 6 cm., and weighed 250 Gm. The surface was covered by masses of fat tissue and strips of reddish-brown muscle. The tissue of the tumor mass was soft and fleshy in character. The tissue was sectioned with ease but contained irregular bone fragments in several areas. On longitudinal section the bulk of the specimen was formed by a mass 9 x 5 x 5 cm. comprised of pale, "fish-flesh" tissue, friable and soft, with irregular areas, dark reddish-brown in color, and of very soft consistency. There was a marginal zone of fibrous and fat tissue and muscle several millimeters to a centimeter in thickness. A layer of tough, firm, white tissue resembling cartilage or fibrocartilage 2 to 3 mm. in thickness was present medially. A short fragment of bone was present on the lateral aspect. A separate fragment of bone 2.5 x 2 x 1.5 cm. was received separately and appeared to articulate with the lateral aspect of the main mass. Except for a purplish-red, soft zone, 0.5 cm. on its medial aspect, this bone fragment was of hard consistency and white color (fig. 1).

Microscopic examination. Sections from all portions of the tumor mass were of marked cellularity and comprised chiefly of cells of small size, rounded, pear-shaped, or polyhedral, and often with eccentrically placed nuclei. The cytoplasm was basophilic, staining shades of lavender to deep purple in hematoxylin and eosin preparations with a small, oval, pale-staining zone adjoining the nucleus in many cells. Nuclei were round to oval, usually of small size, with very coarse but evenly distributed chromatin. Occasionally a single small nucleolus was present. A few cells contained two or more nuclei, each of similar appearance and size and often with a common clear paranuclear zone. Many cells were within the usual limits of size for normal plasma cells, but some were nearly double that size. Nuclei were often of uniform measurement regardless of cell size but in a few instances were almost double the usual diameter of plasma cell nuclei. Rare mitoses were present; no multiple mitoses or tumor giant cells were found. A moderate number of lymphocytes were scattered among the cells described. There was no intercellular matrix. Frequent capillaries and thin-walled vessels were present throughout the tumor, and cells lay in close relation to the endothelium. Occasionally tumor cells were found in these vessels. Patches of hemorrhage and masses of fibrin deposit were present in portions of the tumor. The external configuration of the tumor tissue was irregular as it adjoined dense connective tissue. However, cells did not stream individually into either connective tissue or muscle and were separated from the latter by a zone of fibrous tissue or periosteum. In a rare section this marginal zone of the neoplasm contained small, homogeneous, pink-staining, hyaline masses which stained positively for amyloid with the Mayer's crystal violet method and were adjoined by occasional giant cells of foreign body type. A rare viable bone fragment was present in the connective tissue about the tumor, and occasionally there was slight osteoblastic activity. In sections taken from the sternoclavicular joint aspect the cartilage was preserved. A few foci of lymphocytes and rare typical plasma cells were found in the connective tissue and muscle.

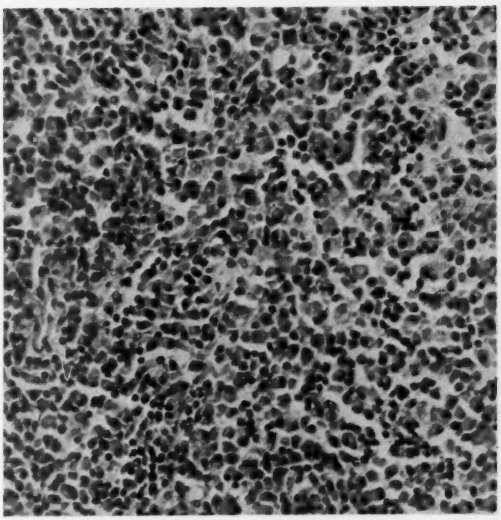

FIG. 2. Photomicrograph showing neoplastic cells with eccentric nuclei and pale staining paranuclear zones. x200.

The pathologic diagnosis was plasmocytoma involving the clavicle and adjoining soft tissue structures (fig. 2).

Postoperative Course

Except for some elevation of the pulse rate and temperature, which returned to normal with penicillin therapy, the postoperative course was uneventful.

Examination of the blood on the ninth postoperative day revealed a red cell count of 3,630,000, hemoglobin 9.0 Gm. per cent, and a white cell count of 9700 with 65 per cent neutrophils, 24 per cent lymphocytes, 8 per cent monocytes, 1 per cent eosinophils, 1 per cent basophils, and 1 per cent metamyelocytes. No abnormal forms were observed, and the platelets were normal. There were 2.9 per cent reticulocytes. A sternal marrow examination revealed cellular marrow with a relative increase in myeloid elements and with a slight shift to the left in this series. Plasma cells were slightly increased to 3.5 per cent and showed moderate pleomorphism, but the majority of nuclei were of mature type and no extremely large forms were seen. Dr. L. W. Diggs examined the marrow and did not regard it as diagnostic.

Roentgenologic examination fourteen days after operation revealed no evidence of myeloma in plates of the skull, lumbar spine, sternum, right hip, and right knee.

No examination of the urine for Bence Jones protein was made at this time.

The patient was discharged on the fifteenth postoperative day and advised to return every three months for check-up.

A roentgenogram of the right clavicle two and one-half months after discharge revealed no evidence of a soft tissue mass in the original site of the clavicle.

Six months after discharge the patient was free of symptoms. Hemoglobin was 12.5 Gm. per 100 cc., the white cell count 8000 with 59 per cent neutrophils.

Nine months after operation a check-up revealed no radiologic evidence of local recurrence in the right clavicular area and no apparent myeloma of the skull, lumbar spine, sternum, or pelvis. X-ray examination of the chest was negative except for absence of the right clavicle. The findings in a sternal marrow examination were essentially as before (2 per cent plasma cells). No Bence Jones protein was demonstrable in the urine. The serum total protein was 6.9 per cent. A sedimentation rate was somewhat increased to 1.0 mm. per minute (normal limit 0.45 mm. per minute). The patient was free of symptoms.

Comments

Plasmocytoma occurring as an apparently solitary lesion without detectable involvement of other bones has been described in many anatomic locations. In 1940 Paul and Pohle[2] reviewed 40 cases from the literature and added 5 of their own. They found the most common locations to be the bones of the pelvis (10 cases), dorsal spine (9 cases), femur (8 cases), and humerus (5 cases), with other recorded locations in the jaw, tibia, cervical region of the spine, skull, and clavicle. The average age of patients was 48 years; two-thirds were of male sex. Unostotic location of the tumor in some of the cases can be only presumptive, as in several instances foci in other bones were recorded only a few months after the original lesion was discovered. Cutler *et al.*[3] divide the solitary plasma cell myelomas into two groups, one in which the primary lesion is followed in several months or several years by typical multiple myeloma and a second group in which the lesion apparently remains solitary. Unfortunately the time of follow-up has been too short to evaluate adequately the course of many of the recorded cases. However, the above authors[3] report 3 patients followed for periods of four, nine, and ten years, respectively, without appearance of tumor in bones other than the primary site. Pasternack and Waugh[4] report a case of solitary myeloma of the humerus under observation seven and one-half years without evidence of generalized bone involvement. Bailey[5] presents a case followed through seven years without diffuse spread. Stewart and Taylor[6] record 2 instances of eight-year survival without evident diffuse skeletal involvement. At the time of first observation there is no means of determining which course these tumors will follow. Diffuse involvement may occur several months or even several years after discovery of the solitary lesion. Jacox and Kahn[7] record a case in which the interval was four and one-half years.

The first manifestation of the lesion may be pain, presence of a mass, or spontaneous fracture. Pasternack and Waugh[4] in a review of 30 cases found pain the presenting symptom in 74 per cent, swelling in 48 per

cent. Tennent[8] found a high percentage of pathologic fractures when the primary lesion occurred in the long bones.

Positive diagnosis of this tumor before histologic examination is difficult. The radiologic appearance is variable, as the lesion may simulate giant cell tumor, bone cyst, metastatic carcinoma, chondroma or chondrosarcoma, and hemangioma of the bone. Generally the diagnosis of giant cell tumor or metastatic carcinoma is made roentgenologically. The excellent review by Paul and Pohle[2] includes detailed discussion of radiologic features. Bence Jones proteinuria usually is absent until there is evidence of polyostotic involvement. Blood protein levels are usually normal. The sedimentation rate is not increased usually until there is diffuse disease. Sternal marrow examination is said to be most valuable. In the presence of generalized involvement there will usually be abnormalities in the percentage and, perhaps, the type of plasma cell, and one report states that the sternal marrow examination may be the only examination of value when the lesion appears to be solitary.[8] Bichel and Kirketerp[9] report an increase in plasma cells of the sternal marrow to 42.2 per cent and 22 per cent, respectively, in 2 cases in which radiologically there were solitary lesions. In these instances there were blood protein changes consistent with multiple myeloma, and in 1 instance Bence Jones protein was also found. They call attention to the fact that diffuse disease may be present even when there appears to be only a single lesion on radiologic examination. In the instance of the present report the plasma cells of the sternal marrow were slightly increased to 3.5 per cent, but this was not regarded as diagnostic. The prognostic importance of such a level cannot yet be judged.

There is an insufficient number of cases reported with adequate follow-up to evaluate therapy properly. The natural history of the disease is such that generalization may not be evident for several years. In a case reported by Tennent[8] in which no treatment was given, two years elapsed before diffuse involvement was observed. Any judgment of therapeutic effectiveness must take this into consideration. Excision or amputation, curettage, radiation therapy, or radiation therapy in addition to one of the above have all at times been associated with survivals of two years or more. For solitary lesions of the extremities Paul and Pohle recommend radiation and state that excision or amputation should be considered in the event of recurrence. For other locations they advocate curettage and radiation, where feasible, or radiation alone. For recurrent lesions after surgical intervention, radiation therapy has shown a palliative effect and perhaps has prolonged life. When used as primary therapy it has relieved pain or other discomfort. The lesion decreases in size but generally does not disappear. In the tabulation of

45 cases by Paul and Pohle there are 9 instances of survival for more than four years. Three of the patients received radiation therapy following curettage or partial resection, 1 was given roentgen therapy after biopsy, and 5 were treated by resection or amputation. In the last group, surgical intervention occurred after radiation in 2 instances. In the case here reported, local surgical excision of the mass was elected and reliance placed on such removal. There has been insufficient time for determination of the result.

Summary

Plasmocytoma of the bone manifested as a solitary lesion is rare but has been established as an entity. Though in many instances the disease has terminated with diffuse involvement of the skeleton, it has been recorded as remaining localized or not recurring for a period of years. Sternal marrow studies may be of aid in the diagnosis or in determining generalization. The lesion is first manifested by pain, swelling, or, as is common in the long bones, spontaneous fracture. Radiologically the solitary lesion most often simulates giant cell tumor or metastatic carcinoma. Resection, when feasible, seems the most logical therapeutic approach. From published reports radiation therapy appears to be of value in the control of recurring lesions and when used primarily may reduce the size of the lesion and alleviate symptoms.

A case of apparently solitary plasmocytoma of the clavicle is presented.

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